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 NEWS 31 Nov 18 DKILIT has been renamed APOLLIT
 NEWS 32 Nov 25 More calculated properties added to REGISTRY
 NEWS 33 Dec 02 TIBKAT will be removed from STN
 NEWS 34 Dec 04 CSA files on STN
 NEWS 35 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
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 NEWS 38 Dec 30 ISMEC no longer available
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 NEWS 40 Jan 21 NUTRACEUT offering one free connect hour in February 2003
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 NEWS 42 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
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COST IN U.S. DOLLARS

SINCE FILE
ENTRY

TOTAL
SESSION

FULL ESTIMATED COST

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0.21

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DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

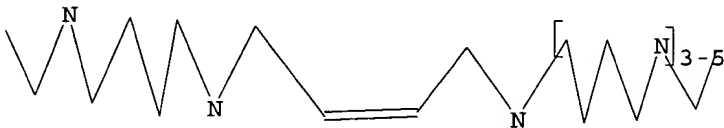
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L1 STR



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=> s l1
SAMPLE SEARCH INITIATED 16:18:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 96 TO ITERATE

100.0% PROCESSED 96 ITERATIONS 1 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1333 TO 2507
PROJECTED ANSWERS: 1 TO 80

L2 1 SEA SSS SAM L1

=> s l1 full
FULL SEARCH INITIATED 16:18:48 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 2348 TO ITERATE

100.0% PROCESSED 2348 ITERATIONS 8 ANSWERS
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L3 8 SEA SSS FUL L1

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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 6 L3
=> d l4 1-6 abs ibib hitstr

AB Polyamine or polyamine analog-amino acid conjugates

(M)-N(E)-(B-A-B-NH)4-E

or (M)-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [M is an amino acid; A is a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B is a bond, alkyl, or alkenyl; E is H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl], including salts or stereoisomers, were prep'd. for use as antiviral agents.

An example is the polyamine glutamine conjugate SL-11165 (NH₂CH(CH₂CH₂CONH₂)CON(Et)(CH₂CH₂CH₂CH₂NH)4Et.bul.5HCl). Thus, (E)-EtNH(CH₂)4NHCH₂CH₂CH₂CH₂CH₂4NHET was prep'd. by a multi-step sequence starting from 4-bromobutanenitrile, N-(mesitylsulfonyl)ethanamine, and (E)-2-butene-1,4-diol.

ACCESSION NUMBER: 2002:888472 CAPLUS

DOCUMENT NUMBER: 137:384565

TITLE: Preparation of polyamine or polyamine analog-amino acid conjugates as antiviral agents

INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.; Gutierrez, Jesus A.

PATENT ASSIGNEE(S): Slll Biomedical Corporation, USA; Eli Lilly & Company

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002091989	A2	20021121	WO 2001-US43887	20011108
W: AB, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPL. INFO.: US 2000-246804P P 20001108				
OTHER SOURCE(S): MARPAT 137:384565				

IT 304911-08-8P, SL 11150

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

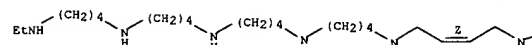
(prepn. of polyamine or polyamine analog-amino acid conjugates as antiviral agents)

RN 304911-08-8 CAPLUS

CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (222)- (9CI) (CA INDEX NAME)

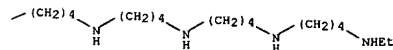
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PAGE 1-A



●10 HCl

PAGE 1-B



IT 304863-19-2P 304863-21-6P 304911-07-7P, SL

11144

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

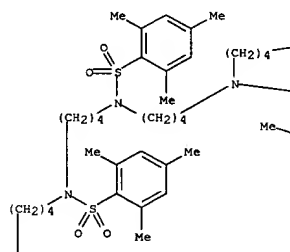
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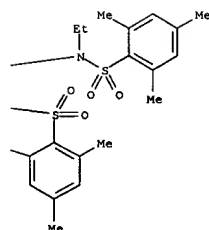
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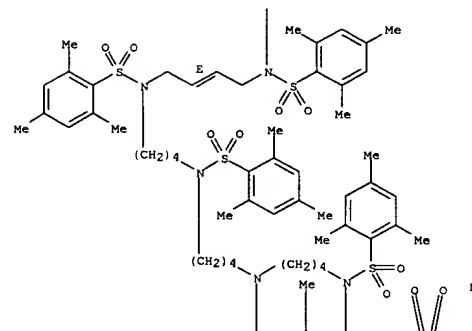
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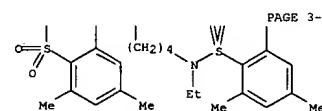
PAGE 1-B



PAGE 2-A



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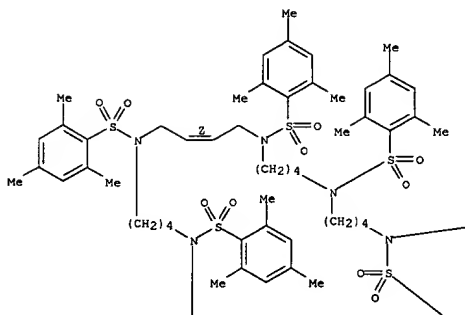


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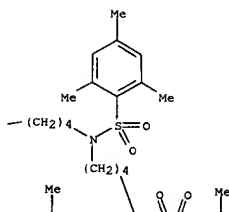
CN Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

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PAGE 1-B



L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS
 AB Conjugates of polyamines analogs conjugated to at least one amino acid of formula M-N(E)-(B-A-B-NH)4-E or M-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [wherein

M = independently an amino acid, esp. glutamine, asparagine, lysine, ornithine, arginine, histidine, or citrulline; A = independently a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B = independently a bond, alkyl, or alkenyl; E = independently H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; and salts or stereoisomers thereof]

were tested and claimed for pharmaceutical use as anticancer agents. For example, the polyamine glutamine conjugate SL-11165 [NH₂CH(CH₂CH₂CONH₂)CON(Et)(CH₂CH₂CH₂CH₂NH)₄Et.bul.5HCl] exhibited ID₅₀ values of >31.65, 4.1, and >31.25 against the DuPro, PC-3, and LnCap prostate cancer cell lines, resp. In addn., conformationally restricted polyamine analogs were prepd. Thus,

(E)-EtNH(CH₂)₄NHCH₂CH₂CH₂CH₂NH(CH₂)₄NH
 Et was prepd. in a multi-step sequence starting from 4-bromobutanenitrile,

N-mesitylethanamine, and (E)-2-butene-1,4-diol.

ACCESSION NUMBER: 2002:368258 CAPLUS

DOCUMENT NUMBER: 136:386292

TITLE: Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as anticancer agents

INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas,

Aldonia L.; Reddy, Venodhar K.

PATENT ASSIGNEE(S): Sili Biomedical Corporation, USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIKXDZ

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

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WO 2002038105	A2	20020516	WO 2001-US43585	20011108
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AU 200203126	A5	20020521	AU 2002-35126	20011108
PRIORITY APPLN. INFO.: US 2000-246804P P 20001108				
WO 2001-US43585 W 20011108				

OTHER SOURCE(S): MARPAT 136:386292

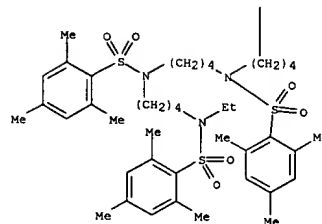
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RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

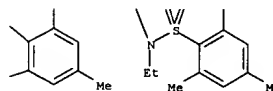
(intermediate; prepn. of conformationally restricted polyamines and

use

PAGE 2-A



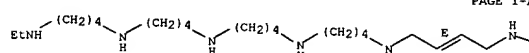
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RN 304911-07-7 CAPLUS
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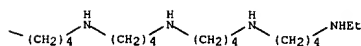
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● 10 HCl

PAGE 1-B



L4 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

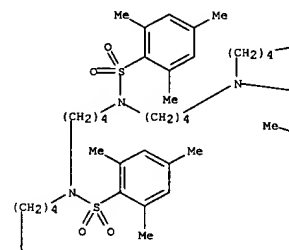
of polyamine amino acid conjugates as anticancer agents)

RN 304863-19-2 CAPLUS

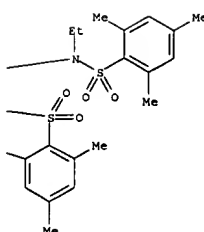
CN Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-(5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

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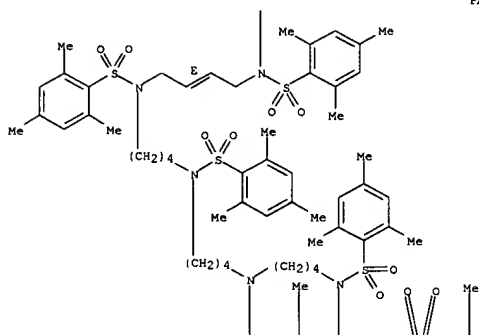
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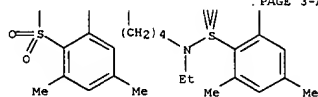
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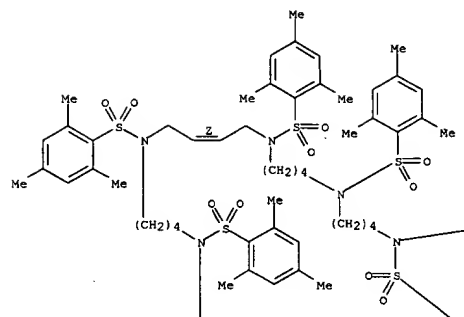
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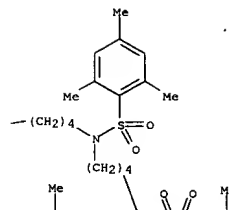
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Double bond geometry as shown.

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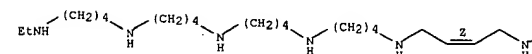
PAGE 1-B



polyamine amino acid conjugates as anticancer agents)
 RN 304911-08-8 CAPLUS
 CN 5,10,15,20,25,30,35,40-Octaazatetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22Z)- (9CI) (CA INDEX NAME)

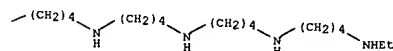
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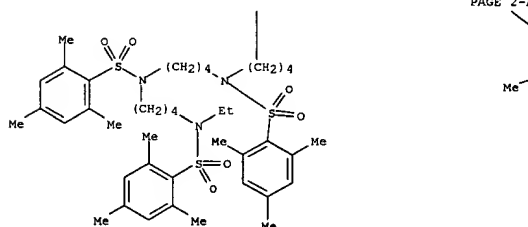


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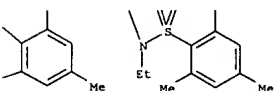
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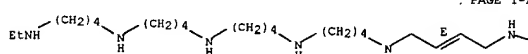
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RN 304911-07-7 CAPLUS
 CN 5,10,15,20,25,30,35,40-Octaazatetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

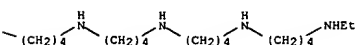
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PAGE 1-B

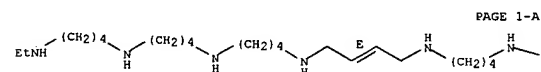


IT 304911-08-8P, SL 11150
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (polyamine; prepn. of conformationally restricted polyamines and use of

L4 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2003 ACS
AB The pre-emergent spore stages of Encephalitozoon cuniculi were evaluated for polyamine uptake and interconversion. The possible effects of SL-11158 on polyamine metab. were also studied. Enc. cuniculi was maintained on RK-13 cells, which were grown to 80% confluency in Corning T-26 or Falcon T-75 flasks and infected with 5 x 10⁵ spores. Enc. cuniculi assimilated and interconverted polyamines; spermidine was taken up far more readily than spermine. A large proportion of the metabolites were excreted as in mammalian cells. The major effects of polyamine analogs on cells include competition for uptake through polyamine transporters, upregulation of spermidine/spermine N1-acetyltransferase, and excretion of polyamines, leading to reductn. of polyamine content. The inhibition of metabolite prodn. and excretion by a low concn. of SL-11158 suggested that this polyamine analog targets, in part, polyamine interconversion in this parasite.

ACCESSION NUMBER: 2002:27765 CAPLUS
DOCUMENT NUMBER: 137:182043
TITLE: SL-11158, a synthetic oligoamine, inhibits polyamine metabolism of Encephalitozoon cuniculi
AUTHOR(S): Bacchi, Cyrus J.; Orozco, Daniel; Weiss, Louis M.; Frydman, Benjamin; Valasinas, Aldonia; Yarleett, Nigel;
CORPORATE SOURCE: Marton, Laurence J.; Wittner, Murray
Haskins Laboratories, Pace University, New York, NY, 10038, USA
SOURCE: Journal of Eukaryotic Microbiology (2001), (Suppl.), 92S-94S
CODEN: JEMIED; ISSN: 1066-5234
PUBLISHER: Society of Protozoologists
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 412351-17-8, SL-11158
RL: BSU (Biological study, unclassified); BIOL (Biological study) (synthetic oligoamine SL-11158 inhibits polyamine metab. of Encephalitozoon cuniculi)
RN 412351-17-8 CAPLUS
CN 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (17E)- (9CI) (CA INDEX NAME)

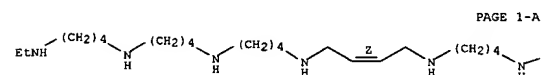
Double bond geometry as shown.



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
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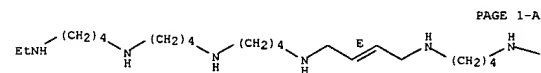
L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)
IT 412351-16-7, SL 11157 412351-17-8, SL 11158
412351-20-3, SL 11172
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)
RN 412351-16-7 CAPLUS
CN 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (17Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



RN 412351-17-8 CAPLUS
CN 5,10,15,20,25,30-Hexaaza-17-tetratriacontene-1,34-diamine, N,N'-diethyl-, (17E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



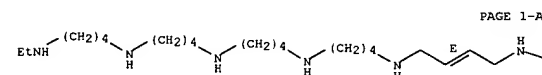
RN 412351-20-3 CAPLUS
CN 5,10,15,20,25,30,35,40,45,50-Decaaza-27-tetrapentacontene-1,54-diamine, N,N'-diethyl-, (27E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

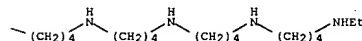
L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS
AB Microsporidia are eukaryotic obligate intracellular protists that are emerging pathogens in immunocompromised hosts, such as patients with AIDS or patients who have undergone organ transplantation. We have demonstrated in vitro and in vivo that synthetic polyamine analogs are effective antimicrosporidial agents with a broad therapeutic window. CD8-knockout mice or nude mice infected with the microsporidian Encephalitozoon cuniculi were cured when they were treated with four different novel polyamine analogs at doses ranging from 1.25 to 5 mg/kg of body wt./day for a total of 10 days. Cured animals demonstrated no evidence of parasitemia by either PCR or histol. staining of tissues 30 days after untreated control animals died.

ACCESSION NUMBER: 2002:30291 CAPLUS
DOCUMENT NUMBER: 136:318859
TITLE: Novel synthetic polyamines are effective in the treatment of experimental microsporidiosis, an opportunistic AIDS-associated infection
AUTHOR(S): Bacchi, Cyrus J.; Weiss, Louis M.; Lane, Schenella; Frydman, Benjamin; Valasinas, Aldonia; Reddy, Venodhar; Sun, Jerry S.; Marton, Laurence J.; Khan, Initiaz A.; Moretto, Magali; Yarleett, Nigel; Wittner, Murray
CORPORATE SOURCE: Haskins Laboratories and Departments of Biology and Chemistry, Pace University, New York, NY, 10038-1598, USA
SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(1), 55-61
CODEN: AMACQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 304911-07-7, SL 11144
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11144; novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)
RN 304911-07-7 CAPLUS
CN 5,10,15,20,25,30,35,40-Octaazatetratriacont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

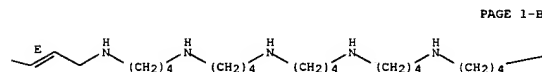
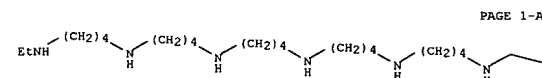
Double bond geometry as shown.



●10 HCl



L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)



—NH₂
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE
FORMAT

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS
AB Novel conformationally restricted polyamines, such as E-NH-(B-A-B-NH)4-E
[A, E = bond, alkyl, alkenyl, cycloalkyl, cycloaryl,
cycloalkenyl; B = bond, alkyl, alkenyl], were prepd. for pharmaceutical
use as anticancer agents. Thus, (E)-EtNH(CH2)4NHCH2CH=CHCH2NH(CH2)4NHET
was prepd. in a multistep sequence starting from mesityl chloride
4-bromobutanenitrile, N-mesitylethanamine, and (E)-2-butene-1,4-diol.

The prepd. polyamines were tested for antiproliferative activity against
human prostate cancer cell lines, such as PC3 and DUPRO.

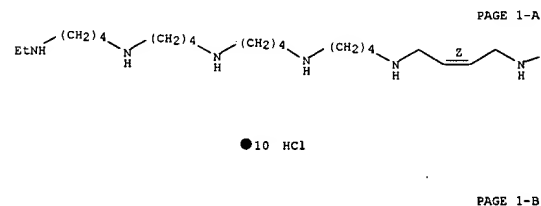
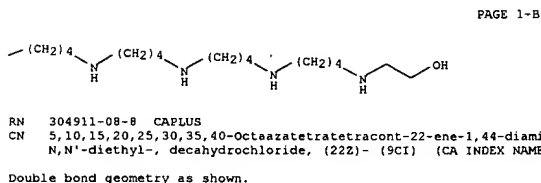
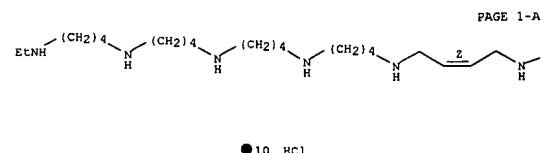
ACCESSION NUMBER: 2000:790505 CAPLUS
DOCUMENT NUMBER: 133:350095
TITLE: Preparation of conformationally restricted polyamine
analogues as disease therapies
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Reddy,
Venodhar K.; Valasinas, Aldonia; Blokhin, Andrei V.;
Basu, Hiral S.
PATENT ASSIGNEE(S): S11 Biomedical Corporation, USA
SOURCE: PCT Int. Appl., 135 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066587	A2	20001109	WO 2000-US11591	20000427
WO 2000066587	A3	20010125		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1177197	A2	20020206	EP 2000-928583	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010701	A	20020213	BR 2000-10701	20000427
JP 2002543202	T2	20021217	JP 2000-615617	20000427
PRIORITY APPLN. INFO.: US 1999-131779P P 19990430 WO 2000-US11591 W 20000427				

OTHER SOURCE(S): MARPAT 133:350095
IT 304863-62-5P 304911-08-0P, SL 11150
RI: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of conformationally restricted polyamines as antiproliferative prostate cancer agents)
RN 304863-62-5 CAPLUS
CN 3,8,13,18,23,28,33,38,43,48-Decaazapentacont-25-en-1-ol, decahydrochloride, (25Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

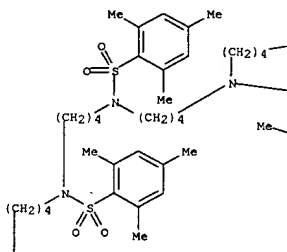
L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)



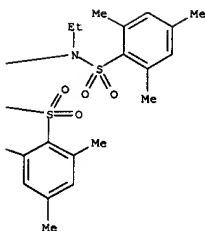
L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

Double bond geometry as shown.

PAGE 1-A

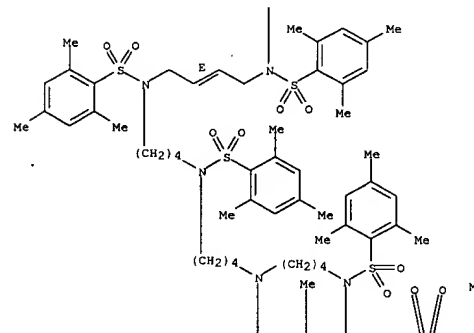


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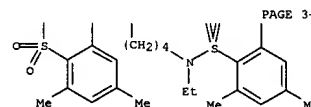


L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2003 ACS (Continued)

PAGE 2-A



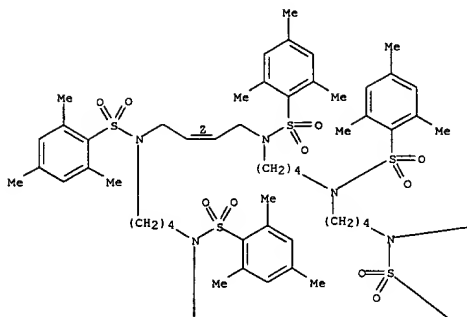
PAGE 3-A



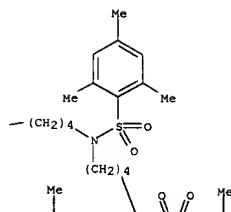
RN 304863-21-6 CAPLUS
CN Benzenesulfonamide, N,N'-(2Z)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



AB The invention relates to peptide conjugates in which cytotoxic and cytostatic agents, such as polyamine analogs or naphthoquinones, are conjugated to a polypeptide recognized and cleaved by enzymes such as prostate-specific antigen (PSA) and cathepsin B. Methods of using these conjugates in the treatment of prostate diseases are also provided.

Thus, C2[CH2NH(CH2)4NHET]2.4HCl (SL-11103), 4-[[7-[4-(9-acridinylamino)phenyl]heptyloxy]-1,2-naphthoquinone (SL-11064), and morpholino-Ser-Lys-Leu-Gln-.beta.-Ala-.beta.-lapachone (SL-11147) were prepd. and assayed for antitumor activity against human prostate cancer cell lines, such as PC-3 and DUPRO.

ACCESSION NUMBER: 2000:790358 CAPLUS
DOCUMENT NUMBER: 133:350515

TITLE: Preparation of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases

INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.

PATENT ASSIGNEE(S): Slll Biomedical Corporation, USA

SOURCE: PCT Int. Appl., 194 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066175	A2	20001109	WO 2000-US11542	20000427
WO 2000066175	A3	20010802		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1173223	A2	20020123	EP 2000-928565	20000427
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BR 2000010700	A	20020213	BR 2000-10700	20000427
JP 2002543163	T2	20021217	JP 2000-615058	20000427
PRIORITY APPLN. INFO.: US 1999-131809P P 19990430				
WO 2000-US11542 W 20000427				

OTHER SOURCE(S): MARPAT 133:350515
IT 304863-19-2P 304863-21-6P 304911-07-7P

304911-09-8P, SL 11150

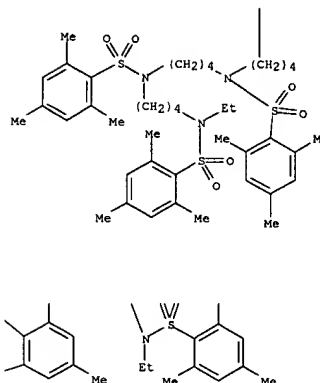
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)

RN 304863-19-2 CAPLUS

CN Benzenesulfonamide, N,N'-(2E)-2-butene-1,4-diylbis[2,4,6-trimethyl-N-[5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 2-A

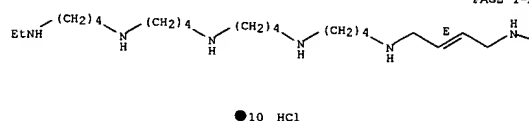


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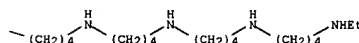
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CN 5,10,15,20,25,30,35,40-Octaazatetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

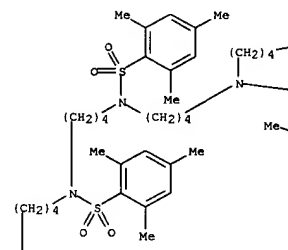
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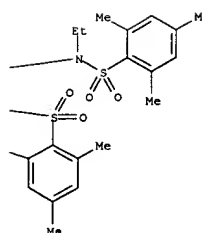
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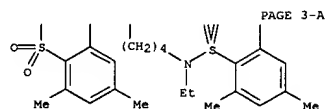
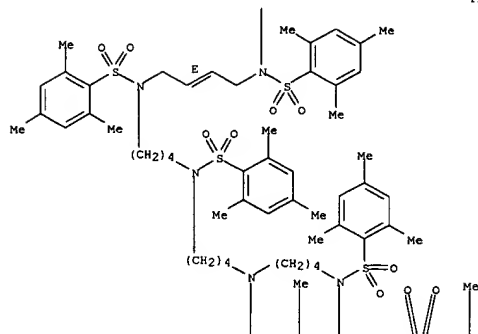
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PAGE 1-B



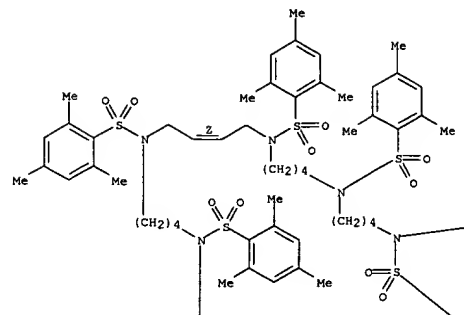
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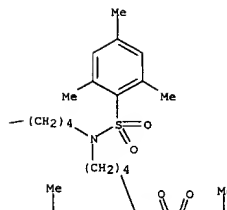
RN 304963-21-6 CAPLUS
 CN Benzenesulfonamide, N,N'-(2Z)-2-butene-1,4-diylbis[2,4,6-trimethyl-5,10,15,20-tetrakis[(2,4,6-trimethylphenyl)sulfonyl]-5,10,15,20-tetraazadocos-1-yl]- (9CI) (CA INDEX NAME)

Double bond geometry as shown.

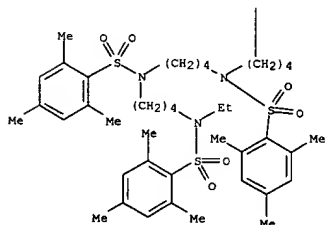
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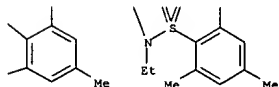
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PAGE 2-A



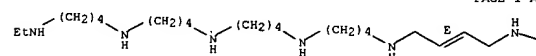
PAGE 2-B



RN 304911-07-7 CAPLUS
 CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22E)- (9CI) (CA INDEX NAME)

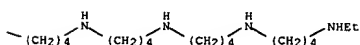
Double bond geometry as shown.

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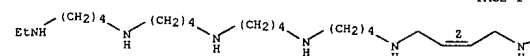
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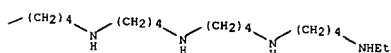
RN 304911-08-8 CAPLUS
 CN 5,10,15,20,25,30,35,40-Octaazatetratetracont-22-ene-1,44-diamine, N,N'-diethyl-, decahydrochloride, (22Z)- (9CI) (CA INDEX NAME)

PAGE 1-A



●10 HCl

PAGE 1-B



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FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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CA SUBSCRIBER PRICE

FILE 'REGISTRY' ENTERED AT 16:22:34 ON 06 FEB 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

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STRUCTURE FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STN Note 27, Searching Properties in the CAS Registry File, for complete details:


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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)  SINCE FILE  TOTAL
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L8 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AB The invention is a series of novel and effective inhibitors of integrase, an essential in the life cycle of retroviruses. These compds. were designed to have a restricted conformation for the detn. of the integrase binding site and mechanism of inhibition. The integrase inhibitors of the invention are effective in the submicromolar range, and thereby provide novel lead compds. for the development of anti-viral therapeutics.

ACCESSION NUMBER: 2002:31406 CAPLUS
 DOCUMENT NUMBER: 136:79737
 TITLE: Symmetric inhibitors of HIV integrase, mammalian topoisomerase and serineprotease
 INVENTOR(S): Harrison, Robert W.; Skalka, Anna Marie
 PATENT ASSIGNEE(S): Thomas Jefferson University, USA
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

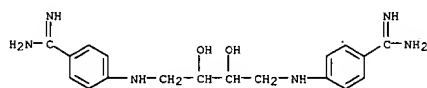
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002002516	A2	20020110	WO 2001-US19923	20010622
WO 2002002516	A3	20021024		

W: CA, JP
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

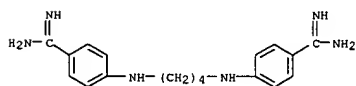
PRIORITY APPLN. INFO.: US 2000-215474P P 20000630

IT 387397-93-SP, RW 23
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
 (sym. inhibitors of HIV integrase, mammalian topoisomerase and serineprotease)

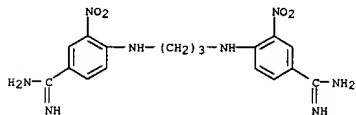
RN 387397-93-5 CAPLUS
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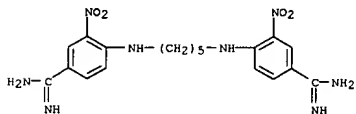
L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)
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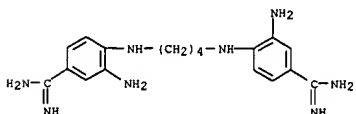
RN 125880-83-3 CAPLUS
 CN Benzenecarboximidamide, 4,4'-[(1,3-propanediyl)diimino]bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-84-4 CAPLUS
 CN Benzenecarboximidamide, 4,4'-[(1,5-pentanediyl)diimino]bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-86-6 CAPLUS
 CN Benzenecarboximidamide, 4,4'-[(1,4-butanediyl)diimino]bis[3-amino- (9CI) (CA INDEX NAME)



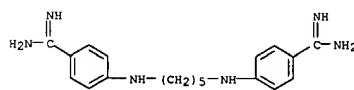
RN 125880-89-9 CAPLUS

L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AB A proposed model for the interaction of bisamidines analogs with the B-DNA receptor is established by structure-property relationship studies derived from 3D-WHIM descriptor calcs. Three classes, each with relevant information about structural relationships, were detd. by PCA and SIMCA analyses for mol. conformations described by 3D-WHIM descriptors for a set of 29 bisamidines with antileishmaniasis and anti-PCP activities. Shape, distribution and dimension properties mostly govern the interaction of bisamidines with B-DNA through the minor groove AT rich regions.

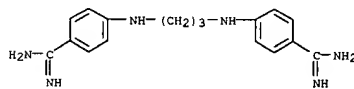
ACCESSION NUMBER: 2000:664385 CAPLUS
 DOCUMENT NUMBER: 133:344182
 TITLE: 3D-WHIM pattern recognition study for bisamidines. A structure-property relationship study
 AUTHOR(S): Menezes, Fabiano A. S.; Montanari, Carlos A.; Bruns, Roy E.
 CORPORATE SOURCE: Departamento de Quimica, Universidade Federal de Minas
 SOURCE: Gerais, Belo Horizonte, 31270-901, Brazil
 Journal of the Brazilian Chemical Society (2000), 11(4), 393-397
 CODEN: JOCSET; ISSN: 0103-5053
 PUBLISHER: Sociedade Brasileira de Quimica
 DOCUMENT TYPE: Journal
 LANGUAGE: English

IT 124076-63-7 125880-81-1 125880-82-2
 125880-83-3 125880-84-4 125880-86-6
 125880-89-9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (3D-WHIM pattern recognition and structure-activity relationship study for bisamidines)

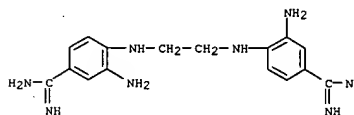
RN 124076-63-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-[(1,5-pentanediyl)diimino]bis- (9CI) (CA INDEX NAME)



RN 125880-81-1 CAPLUS
 CN Benzenecarboximidamide, 4,4'-[(1,3-propanediyl)diimino]bis- (9CI) (CA INDEX NAME)



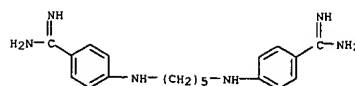
L8 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)
 CN Benzenecarboximidamide, 4,4'-[(1,2-ethanediyl)diimino]bis[3-amino- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

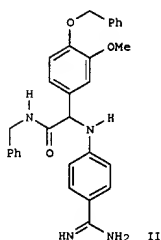
L8 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AB Arom. dicationic drugs have a broad spectrum of activity against
 protozoal
 and fungal pathogens including *Pneumocystis carinii*, *Leishmania mexicana*
amazonensis, *Cryptosporidium parvum*, and *Cryptococcus neoformans*.
 Pentamidine serves as the exemplar for an extensive collection of newly
 synthesized related compds., which have reduced toxicity and a wider
 range
 of target organisms. Assays of pentamidine and related compds. have
 depended on HPLC-tandem mass spectrometry (HPLC-TMS) for the quantitation
 and identification of drug and metabolites. Immunoassays for pentamidine
 would have many advantages over the HPLC methods including relative
 simplicity of assay format and required equipment, convenience in sample
 prepn. and redn. in time and cost of assays. In this report the authors
 describe a simple ELISA based immunoassay for pentamidine and
 pentamidine-like drugs with requisite sensitivity and specificity for use
 as a clin. assay (EC50 value of about 50 nanomolar). Immunogen was
 synthesized by coupling the hapten aminopentamidine to ovalbumin (chem.
 modified to provide an optimal no. of -SH groups) using sulfo-MBS.
 Maleic-anhydride activated ELISA plates were covalently sensitized using
 the amino-pentamidine hapten and used in an inhibitory ELISA assay format
 whereby the ability of analyte to suppress antibody binding to sensitized
 plate was measured. The assay detects primarily the phenolic amidine of
 pentamidine when in a para position and hence can also detect
 structurally
 related derivs. of pentamidine of potential interest as new therapeutic
 agents.
 ACCESSION NUMBER: 2000:204083 CAPLUS
 DOCUMENT NUMBER: 133:114510
 TITLE: Immunoassays for pentamidine and related compounds:
 development of a facile inhibitory ELISA suitable for
 clinical use
 AUTHOR(S): Reisner, Howard M.; Gray, Danny R.; Jones, Susan K.;
 Rose, Beate G.; Tidwell, Richard R.
 CORPORATE SOURCE: Department of Pathology and Laboratory Medicine,
 School of Medicine, University of North Carolina at
 Chapel Hill, Chapel Hill, NC, 27599-7525, USA
 SOURCE: Journal of Clinical Laboratory Analysis (2000),
 14(2),
 73-82
 CODEN: JCANEM; ISSN: 0887-8013
 PUBLISHER: Wiley-Liss, Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 124076-63-7
 RL: BAC (Biological activity or effector, except adverse); BOC
 (Biological
 occurrence); BSU (Biological study, unclassified); THU (Therapeutic use);
 BIOL (Biological study); OCCU (Occurrence); USES (Uses)
 (immunoassays for pentamidine and related compds.)
 RN 124076-63-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA
 INDEX
 NAME)

L8 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR
 THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS
 GI

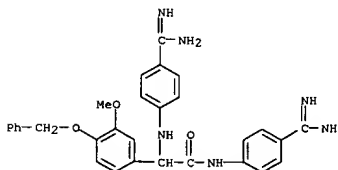


AB RR1NCOCHR2NH2C(:NG1)NHG2 [I: 1 of G1,G2 = H and the other = H, OH, alkyl,
 alkoxy, etc.; R = (un)substituted alkyl, cycloalkyl, aryl; R1 = H or
 alkyl; R2 = (un)substituted Ph or -pyridyl; Z = (3-hydroxy)
 1,4-phenylene]
 were prepd. Thus, 3,4-(MeO)(PhCH2O)C6H3CHO, 4-(H2N)C6H4C(:NH)NH2, and
 PhCH2NHC were condensed to give, after acidification, title compd. II.HCl.
 Data for biol. activity of I were given.
 ACCESSION NUMBER: 1999:375282 CAPLUS
 DOCUMENT NUMBER: 131:44656
 TITLE: Preparation of N-(4-aminophenyl)phenylglycineamides
 as factor VIIa/tissue factor inhibitors
 INVENTOR(S): Grobke, Katrin; Ji, Yu-hua; Wallbaum, Sabine; Weber,
 Lutz
 PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
 SOURCE: Eur. Pat. Appl., 46 pp.
 CODEN: EPXKDW
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 921116	A1	19990609	EP 1998-122169	19981126
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6140353	A	20001031	US 1998-204373	19981202
ZA 9811077	A	19990604	ZA 1998-11077	19981203
NO 9805646	A	19990607	NO 1998-5646	19981203
AU 9895210	A1	19990624	AU 1998-95210	19981203
AU 739769	B2	20011018		
CN 1224714	A	19990804	CN 1998-126979	19981204
JP 11246507	A2	19990914	JP 1998-345875	19981204
JP 3236267	B2	20011210		
BR 9805320	A	20000411	BR 1998-5320	19981204

L8 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)

PRIORITY APPLN. INFO.: EP 1997-121285 A 19971204
 EP 1998-121374 A 19981110
 OTHER SOURCE(S): MARPAT 131:44656
 IT 227021-08-1P
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of N-(4-aminophenyl)phenylglycineamides as factor
 VIIa/tissue
 factor inhibitors)
 RN 227021-08-1 CAPLUS
 CN Benzeneacetamide, N-[4-(aminoiminoethyl)phenyl]-.alpha.-[4-(
 aminoiminoethyl)phenyl]amino]-3-methoxy-4-(phenylmethoxy)-, acetate
 (9CI) (CA INDEX NAME)
 CM 1
 CRN 227021-07-0
 CMF C30 H30 N6 O3



CM 2
 CRN 64-19-7
 CMF C2 H4 O2



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE RE
 FORMAT

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

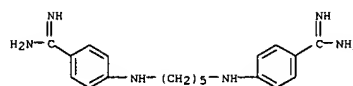
AB Twenty analogs of pentamidine (including I), 7 primary metabolites of pentamidine, and 30 dicationic substituted bisbenzimidazoles were screened for their inhibitory and fungicidal activities against *Candida albicans* and *Cryptococcus neoformans*. A majority of the compds. had MICs at which 80% of the strains were inhibited (MIC80s) comparable to those of amphotericin B and fluconazole. Unlike fluconazole, many of these compds., such as II and III, were found to have potent fungicidal activity. The most potent compd. against *C. albicans* had an MIC80 of .10 to .09 .mu.g/mL, and the most potent compd. against *C. neoformans* had an MIC80 of 0.19 .mu.g/mL. Selected compds., such as IV, were also found to be active against *Aspergillus fumigatus*, *Fusarium solani*, *Candida* species other than *C. albicans*, and fluconazole-resistant strains of *C. albicans* and *C. neoformans*. It is clear from the data presented here that further studies on the structure-activity relationships, mechanisms of action and toxicities, and in vivo efficacies of these compds. are warranted to det. their clin. potential.

ACCESSION NUMBER: 1998:664985 CAPLUS
DOCUMENT NUMBER: 130:22732
TITLE: Structure-in vitro activity relationships of pentamidine analogs and dication-substituted bis-benzimidazoles as new antifungal agents
AUTHOR(S): Del Poeta, Maurizio; Schell, Wiley A.; Dykstra, Christine C.; Jones, Susan; Tidwell, Richard R.; Czarny, Agnieszka; Bajic, Miroslav; Bajic, Marina; Kumar, Arvind; Boykin, David; Perfect, John R.
CORPORATE SOURCE: Department of Medicine, Division of Infectious Diseases and International Health, Duke University Medical Center, Durham, NC, 27710, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(10), 2495-2502
CODEN: AMACQ; ISSN: 0066-4804

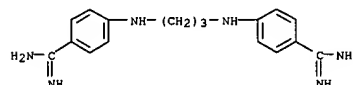
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 124076-63-7 125880-81-1 125880-83-3 125880-85-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(structure-in vitro activity relationships of pentamidine analogs and dication-substituted bis-benzimidazoles as new antifungal agents)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

AB Arom. dicationic compds., such as pentamidine, have potent antimicrobial activities. Clin. use of these compds. has been restricted, however, by their toxicity and limited oral activity. A novel approach, using amidoxime derivs. as prodrugs, has recently been proposed to overcome these limitations. Although results were presented for amidoxime derivs. of only one diamidine, pentamidine, the authors in the original proposal claimed that amidoxime derivs. would work as effective prodrugs for all pharmacol. active diamidines. Nine novel amidoxime derivs. were synthesized and tested in the present study for activity against *Pneumocystis carinii* in corticosteroid-suppressed rats. Only three of the nine compds. had significant oral anti-*Pneumocystis* activity. The bisbenzamidoxime derivs. of three direct pentamidine analogs had excellent oral and i.v. activities and reduced acute host toxicity. These compds. are not likely candidates for future drug development, however, because they have chronic toxic effects and the active amidine compds. have multiple sites susceptible to oxidative metab., which complicates their pharmacol. and toxicol. Novel diamidoximes from three other structural classes, contg. different groups linking the cationic moieties, lacked significant oral or i.v. anti-*Pneumocystis* activity, even though the corresponding diamidines were very active i.v. Both active and inactive amidoximes were readily metabolized to the corresponding amidines by cell-free liver homogenates. Thus, the amidoxime prodrug approach may provide a strategy to exploit the potent antimicrobial and other pharmacol. activities of selected, but certainly not all, arom. diamidines.

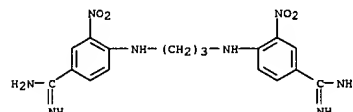
ACCESSION NUMBER: 1998:189774 CAPLUS
DOCUMENT NUMBER: 128:303628
TITLE: Anti-*Pneumocystis* activities of aromatic diamidoxime prodrugs
AUTHOR(S): Hall, James Edwin; Kerrigan, John E.; Ramachandran, Kishore; Bender, Brendan C.; Stanko, Jason P.; Jones, Susan K.; Patrick, Donald A.; Tidwell, Richard R.
CORPORATE SOURCE: Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(3), 666-674
CODEN: AMACQ; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 206532-33-4P
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(anti-*Pneumocystis* activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)
RN 206532-33-4 CAPLUS
CN Propanediamide, N,N'-bis[4-[(hydroxyamino)iminomethyl]phenyl]- (9CI) (CA INDEX NAME)



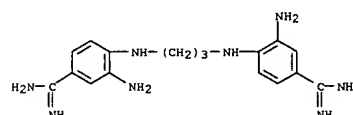
RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)



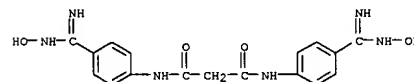
RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



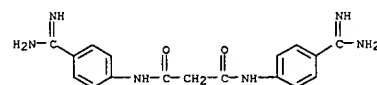
RN 125880-85-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT



IT 206532-34-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-*Pneumocystis* activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)
RN 206532-34-5 CAPLUS
CN Propanediamide, N,N'-bis[4-[(hydroxyamino)iminomethyl]phenyl]- (9CI) (CA INDEX NAME)



L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AB Results are presented for a QSAR anal. of bisamidines, using a similarity index as descriptor. The method allows for differences in conformation

of bisamidines at the receptor site to be taken into consideration. In particular, it has been suggested by others that pentamidine binds in the minor groove of DNA in a so-called isohelical conformation, and the authors QSAR supports this suggestion. The mol. similarity index for comparison of mols. can be used as a parameter for correlating and hence rationalizing the activity as well as suggesting the design of bioactive mols. The studied compds. had been evaluated for potency against Leishmania mexicana amazonensis, and this potency was used as a dependent variable in a series of QSAR analyses. For the calcn. of similarity indexes, each analog was in turn superimposed on a chosen lead compd. in

a ref. conformation, either extended or isohelical, maximizing overlap and hence similarity by flexible fitting.

ACCESSION NUMBER: 1996:162810 CAPLUS
 DOCUMENT NUMBER: 124:277974
 TITLE: Determination of receptor-bound drug conformations by QSAR using flexible fitting to derive a molecular similarity index

AUTHOR(S): Montanari, C. A.; Tute, M. S.; Beezer, A. E.; Mitchell, J. C.

CORPORATE SOURCE: Chem. Lab., Univ. Kent, Canterbury, Kent, CT2 7NH, UK
 SOURCE: Journal of Computer-Aided Molecular Design (1996), 10(1), 67-73
 CODEN: JCADEQ; ISSN: 0920-654X

PUBLISHER: ESCOM
 DOCUMENT TYPE: Journal
 LANGUAGE: English

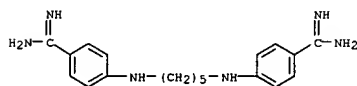
IT 124076-63-7 125000-01-1 125000-02-2
 125000-03-3 125000-04-4 125000-06-6
 125000-07-7 125000-09-9

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (detn. of receptor-bound drug conformations on DNA by QSAR using flexible fitting to derive a mol. similarity index using bisamidines

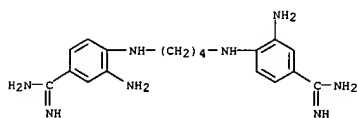
as Leishmania inhibitors)

RN 124076-63-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

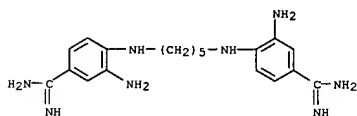


RN 125880-81-1 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA INDEX NAME)

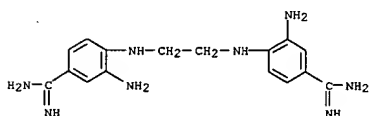
L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



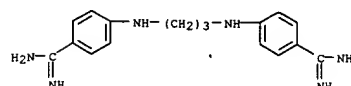
RN 125880-87-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



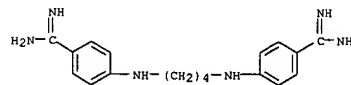
RN 125880-89-9 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



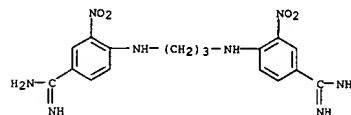
L8 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



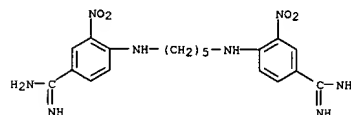
RN 125880-82-2 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-84-4 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



RN 125880-86-6 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

L8 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB The in vitro culture system is described in which Trypanosoma brucei rhodesiense (LOUTat.1) was grown with the human feed layer cell HL-60. The use of this system in detg. the 50% growth Inhibitory Conc. (IC50)

of unknown compds. for both the trypanosomes and the host cell was demonstrated. The data shows that several analogs of pentamidine have significantly reduced host cell toxicity but maintain or have increased trypanocidal activity. The value of the trypanosome/HL-60 in vitro culture system as a rapid primary in vitro drug screen is discussed. Based upon the ability of this primary screen to predict potential drug efficacy, several analogs screened in vitro were then tested in vivo.

The results of the in vivo tests confirmed the ability of the in vitro screen to predict drug efficacy, and also suggests that better analogs of pentamidine (less host toxicity and greater trypanocidal activity) can be obtained to treat human trypanosomiasis.

ACCESSION NUMBER: 1996:138520 CAPLUS
 DOCUMENT NUMBER: 124:249761
 TITLE: The in vitro HL-60 cell - Trypanosoma brucei rhodesiense culture system: A rapid in vitro drug screen

AUTHOR(S): Keku, T. O.; Seed, J. R.; Tidwell, R. R.
 CORPORATE SOURCE: Department of Medicine, University North Carolina, Chapel Hill, NC, USA

SOURCE: Tropical Medicine and Parasitology (1995), 46(4), 258-62
 CODEN: TMPAEY; ISSN: 0177-2392

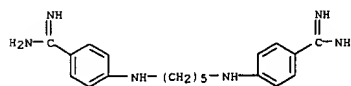
PUBLISHER: Thieme
 DOCUMENT TYPE: Journal
 LANGUAGE: English

IT 124076-63-7
 RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(in vitro HL-60 cell-Trypanosoma brucei rhodesiense culture system for rapid in vitro trypanocidal drug screening)

RN 124076-63-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



L8 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB A mol. mechanics and mol. dynamics approach has been used to examine the structure of the complex formed between pentamidine and the d(CGCGAATTCGCG)2 duplex. Similar energy calcons. have also been performed on complexes with closely related pentamidine analogs, using the complex with the parent drug as the starting point. The resulting structures of the drug-DNA complexes and their energetics have been examd. and are compared with the reported DNA binding affinities. These studies provide rationalizations for the differences in binding behavior of pentamidine analogs with differing linker chain lengths and arom. ring substitutions.

ACCESSION NUMBER: 1993:573590 CAPLUS

DOCUMENT NUMBER: 119:173590

TITLE: DNA minor groove recognition properties of pentamidine

AUTHOR(S): and its analogs: A molecular modeling study
Greenidge, Paulette A.; Jenkins, Terence C.; Neidle, Stephen

CORPORATE SOURCE: Cancer Res. Campaign Biomol. Struct. Unit, Inst.
Cancer Res., Sutton/Surrey, SM2 5NG, UK

SOURCE: Molecular Pharmacology (1993), 43(6), 982-8
CODEN: MOPMA3; ISSN: 0026-895X

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 124076-63-7

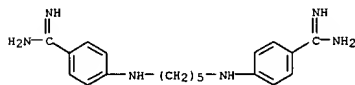
RI: BIOL (Biological study)

(DNA minor groove recognition properties of, anti-Pneumocystis carinii activity in relation to)

RN 124076-63-7 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

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L8 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB We have investigated the interactions of six analogs of pentamidine with the N-methyl-D-aspartate (NMDA) receptor complex. All six compds. were effective NMDA receptor antagonists based upon their ability to inhibit [3H]dizocilpine binding to rat brain membranes. IC50 values ranged from

2

to 18 .mu.M, and all compds. had Hill coeffs. in excess of 1 suggesting a non-competitive interaction with [3H]dizocilpine. All compds. also inhibited NMDA- and glycine-induced intracellular Ca2+ changes measured

in

cultured rat forebrain neurons using the fluorescent indicator, fura-2. IC50 values in this assay ranged from 0.4 to 4.7 .mu.M. Whereas pentamidine is directly toxic to cultured neurons, this was not a consistent finding with the pentamidine analogs tested, indicating that the toxic effects are not related to NMDA receptor antagonism. Finally, all of the agents tested were also effective in protecting neurons from NMDA-induced neurotoxicity. These data emphasize the possible utility of pentamidine-like drugs as neuroprotective agents and suggest that it is possible to generate compds. with a wider margin of safety than pentamidine itself.

ACCESSION NUMBER: 1993:160558 CAPLUS

DOCUMENT NUMBER: 118:160558

TITLE: Studies on the effects of several pentamidine analogs on the NMDA receptor

AUTHOR(S): Reynolds, Ian J.; Zeleski, Diane M.; Rothermund, Kristi D.; Hartnett, Karen A.; Tidwell, Richard; Aizenman, Elias

CORPORATE SOURCE: Dep. Pharmacol., Univ. Pittsburgh, Pittsburgh, PA, 15261, USA

SOURCE: European Journal of Pharmacology, Molecular Pharmacology Section (1993), 244(2), 175-9

CODEN: EJPFET; ISSN: 0922-4106

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 124076-63-7

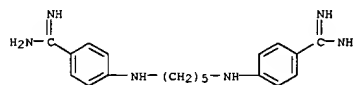
RI: BIOL (Biological study)

(NMDA receptor antagonism by, neurotoxicity and neuroprotective activity in relation to)

RN 124076-63-7 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

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NAME)



L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB The error of omitting the supplementary material available paragraph has been cor. The error was not reflected in the abstr. or the index entries.

ACCESSION NUMBER: 1993:51883 CAPLUS

DOCUMENT NUMBER: 118:51883

TITLE: Structure and DNA binding activity of analogs of 1,5-bis(4-aminophenoxy)pentane (pentamidine). [Erratum to document cited in C116(9):75694b]

AUTHOR(S): Cory, Michael; Tidwell, Richard R.; Fairley, Terri A.

CORPORATE SOURCE: Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA

SOURCE: Journal of Medicinal Chemistry (1992), 35(25), 4767

CODEN: JMCMAR; ISSN: 0022-2623

DOCUMENT TYPE: Journal

LANGUAGE: English

IT 124076-63-7 125880-81-1 125880-82-2

125880-83-3 125880-84-4 125880-85-5

125880-86-6 125880-87-7 125880-89-9

RI: BAC (Biological activity or effector, except adverse); BSU

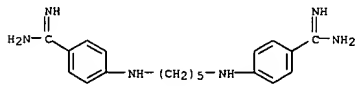
(Biological study, unclassified); BIOL (Biological study)

(DNA-binding activity of (Erratum))

RN 124076-63-7 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA

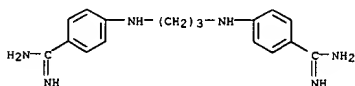
INDEX
NAME)



RN 125880-81-1 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis- (9CI) (CA

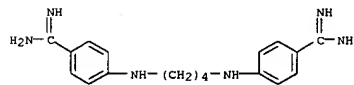
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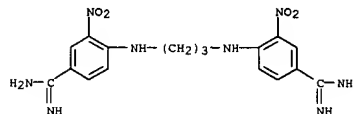
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX
NAME)

L8 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



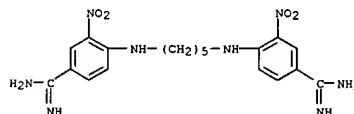
RN 125880-83-3 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



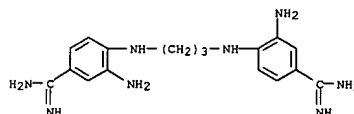
RN 125880-84-4 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



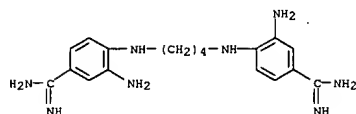
RN 125880-85-5 CAPLUS

CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

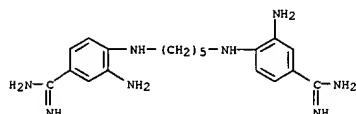


RN 125880-86-6 CAPLUS

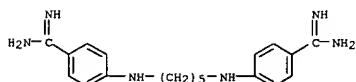
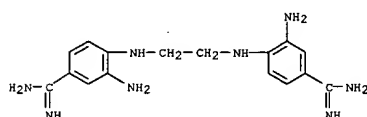
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)



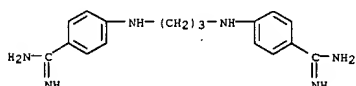
RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-amino- (9CI)
(CA INDEX NAME)



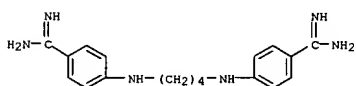
RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis(3-amino- (9CI)
(CA INDEX NAME)



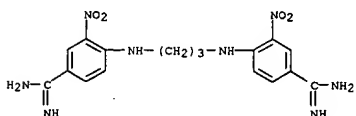
RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis(3-nitro- (9CI) (CA INDEX NAME)



RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis(3-amino- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis(3-nitro- (9CI)
(CA INDEX NAME)

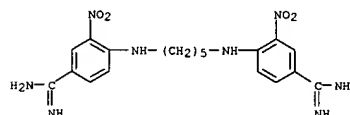


RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-nitro- (9CI)
(CA INDEX NAME)

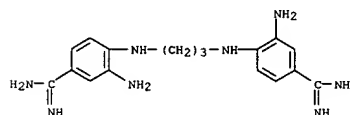
AB The DNA binding properties of a series of bisbenzamides related to the clin. used antipneumocystis drug pentamidine (I) were studied. Changes in the thermal denaturation temp. of calf thymus DNA (.DELTA.Tm) showed that all the compds. have significant affinity for DNA. A comparison of .DELTA.Tms for the series with .DELTA.Tms of base-pair-specific DNA-binding compds., using homopolymers poly(dA).cntdot.poly(dT) and poly(dG-dC).cntdot.poly(dG-dC), indicated that the compds. show moderate specificity for AT base pairs. Lack of DNA helix extension, measured by viscometric titrn. with sonicated calf thymus DNA, indicated that the compds. do not bind to DNA by intercalation. Analogs of I with an odd

no. of methylenes connecting the benzamidine rings had a higher affinity for DNA and homopolymers than analogs with an even no. of methylenes. All of the compds. contg. an amidino group meta to the linking chain showed lower polynucleotide affinity. These results suggest that the shape of the mols. was important for DNA binding. Mol. modeling studies showed a correlation between the DNA binding and the radius of curvature of mol. mechanics models of the mols. Monosubstitution on the benzamidine rings or replacement of the amidino group with the cyclic imidazolino group had no influence on the DNA-binding affinity of the compds. Substitution of NH for the ether oxygen connecting group of I had no effect on the DNA binding or base-pair specificity. Methylation of either of the nitrogen atoms of the imidazolino group to provide an analog of I with N-methylimidazolino groups decreased DNA affinity considerably. GC vs AT base-pair specificity as measured by .DELTA.Tm does not correlate with the radius of curvature. The exptl. and modeling results are consistent with DNA minor-groove binding.

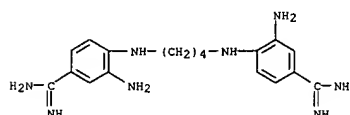
ACCESSION NUMBER: 1992:75694 CAPLUS
DOCUMENT NUMBER: 116:75694
TITLE: Structure and DNA binding activity of analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine)
AUTHOR(S): Cory, Michael; Tidwell, Richard R.; Fairley, Terri A.
CORPORATE SOURCE: Div. Org. Chem., Burroughs Wellcome Co., Research Triangle Park, NC, 27709, USA
SOURCE: Journal of Medicinal Chemistry (1992), 35(3), 431-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 124076-63-7 125880-81-1 125880-82-2
125880-83-3 125880-84-4 125880-85-5
125880-86-6 125880-87-7 125880-89-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (DNA-binding activity of)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-amino- (9CI) (CA INDEX NAME)



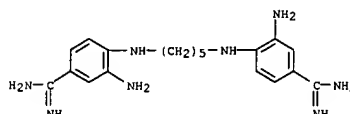
RN 125880-85-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis(3-amino- (9CI)
(CA INDEX NAME)



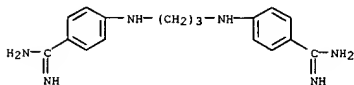
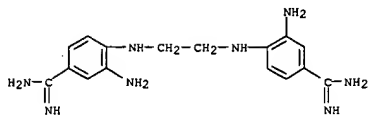
RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis(3-amino- (9CI)
(CA INDEX NAME)



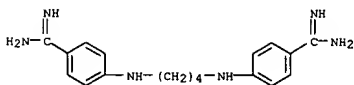
RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis(3-amino- (9CI)
(CA INDEX NAME)



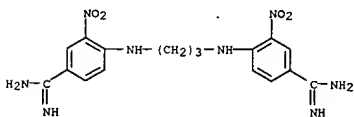
RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis(3-amino- (9CI)
(CA INDEX NAME)



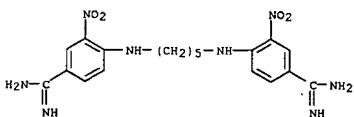
RN 125880-82-2 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyl)bis- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyl)bis[3-nitro- (9CI) (CA INDEX NAME)



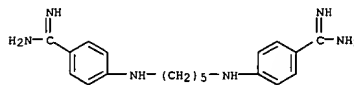
RN 125880-84-4 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



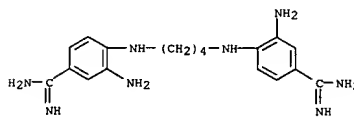
RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediyl)bis[3-amino- (9CI) (CA INDEX NAME)

AB 1,5-Di(4-aminophenoxy)pentane (pentamidine) and 38 analogs of pentamidine were screened for in vitro against the enteric protozoan *Giardia lamblia* WB (ATCC 30957). All compds. were active against *G. lamblia* as measured by a [methyl-3H]thymidine incorporation assay. Antigiardial activity varied widely, with 50% inhibitory concns. (IC50s) ranging from 0.51 +/- 0.13 .mu.M (mean +/- std. deviation) for the most active compd. to over 100.0 .mu.M for the least active compds. The IC50 of the most potent anti-giardial agent, 1,3-di(4-aminophenoxy)propane compared favorably with the IC50s of the compds. currently used to treat giardiasis, i.e., furazolidone (1.0 +/- 0.03 .mu.M), metronidazole (2.1 +/- 0.80 .mu.M), quinacrine HCl (0.03 +/- 0.02 .mu.M), and tinidazole (0.78 +/- 0.48 .mu.M). A mode of anti-giardial activity for these compds. was suggested by the correlation obsd. between anti-giardial activity and the binding of the compds. to calf

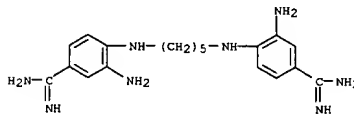
thymus DNA and poly(dA).poly(dT).
ACCESSION NUMBER: 1991:554848 CAPLUS
DOCUMENT NUMBER: 115:154848
TITLE: Structure-activity relationships of pentamidine analogs against *Giardia lamblia* and correlation of anti-giardial activity with DNA-binding affinity
AUTHOR(S): Bell, Constance A.; Cory, Michael; Fairley, Terri A.; Hall, James Edwin; Tidwell, Richard R.
CORPORATE SOURCE: Sch. Public Health, Univ. North Carolina, Chapel Hill,
NC, 27599, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1991), 35(6), 1099-107
CODEN: AMACQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 124076-63-7 125880-81-1 125880-82-2
125880-83-3 125880-84-4 125880-86-6
125880-87-7 125880-89-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (anti-giardial activity of, structure in relation to)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



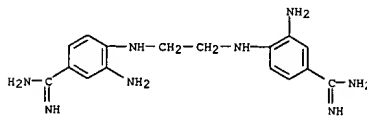
RN 125880-81-1 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediyl)bis- (9CI) (CA INDEX NAME)



RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino- (9CI) (CA INDEX NAME)

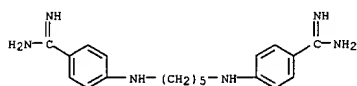


RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyl)bis[3-amino- (9CI) (CA INDEX NAME)



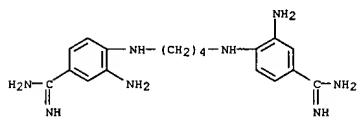
L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AB The antiprotozoal compd. 1,5-di(4-amidinophenoxy)pentane (pentamidine)
 and
 36 of its analogs were screened for in vitro activity against *L. mexicana* amazonensis clone 669 C45 (MHOM/BR/73M2269) and *P. falciparum* clones W2 (Indochina III/CDC) and D6 (Sileira Leone I/CDC). Pentamidine and each of the analogs tested exhibited activity in vitro against *L. mexicana* amazonensis and *P. falciparum*. The pentamidine analogs were more effective against the *P. falciparum* clones than against *L. mexicana* amazonensis. *P. falciparum* was extremely susceptible to these compds., with 50% inhibitory concns. as low as 0.03 μ M. While none of the analogs exhibited marked improvement in antileishmanial activity compared with pentamidine, 12 of the pentamidine analogs showed activity approx. equal to or greater than that of the parent compd. From the promising activity exhibited by the pentamidine analogs in this in vitro study and their potential for reduced toxicity relative to the parent drug, pentamidine-related compds. hold promise as new agents for the treatment of protozoal infections.

ACCESSION NUMBER: 1990:584205 CAPLUS
 DOCUMENT NUMBER: 113:184205
 TITLE: Structure-activity relationships of analogs of pentamidine against *Plasmodium falciparum* and *Leishmania mexicana amazonensis*
 AUTHOR(S): Bell, Constance A.; Hall, James Edwin; Kyle, Dennis E.; Grogl, Max; Ohemeng, Kwasi A.; Allen, Margaret A.; Tidwell, Richard R.
 CORPORATE SOURCE: Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27599, USA
 SOURCE: Antimicrobial Agents and Chemotherapy (1990), 34(7), 1381-6
 CODEN: AMACQ; ISSN: 0066-4804
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 IT 124076-63-7 125880-81-1 125880-82-2
 125880-83-3 125880-84-4 125880-86-6
 125880-87-7 125880-89-9
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (antiprotozoal activity of, against *Plasmodium falciparum* and *Leishmania mexicana amazonensis*, structure in relation to)
 RN 124076-63-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)

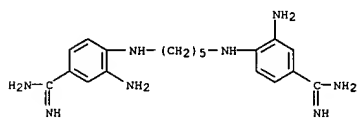


RN 125880-81-1 CAPLUS
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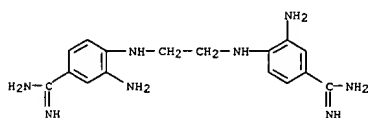
L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



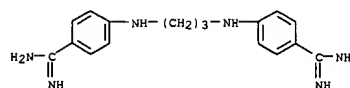
RN 125880-87-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-amino-] (9CI) (CA INDEX NAME)



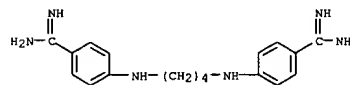
RN 125880-89-9 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,2-ethanediyldiimino)bis[3-amino-] (9CI) (CA INDEX NAME)



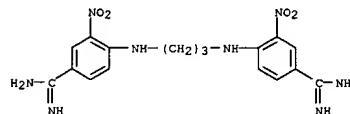
L8 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)



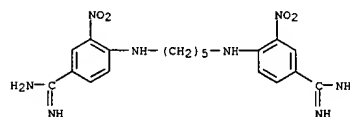
RN 125880-82-2 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis- (9CI) (CA INDEX NAME)



RN 125880-83-3 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro-] (9CI) (CA INDEX NAME)

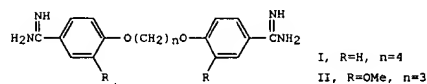


RN 125880-84-4 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro-] (9CI) (CA INDEX NAME)



RN 125880-86-6 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,4-butanediyldiimino)bis[3-amino-] (9CI) (CA INDEX NAME)

L8 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2003 ACS
 GI



AB A series of 33 analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine) was synthesized for screening against a rat model of *P. carinii* pneumonia.

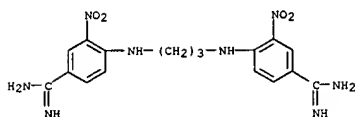
Twenty-five of the compds. showed efficacy against *P. carinii* pneumonia when compared to a saline-treated control group. Two compds., butamidine (I) and 1,3-bis(4-amidino-2-methoxyphenoxy)propane (II), were more effective than pentamidine in treating *P. carinii* pneumonia in the rat model of infection. In addn. to their activity against *P. carinii* pneumonia, the compds. were also evaluated for antitrypsin activity, ability to inhibit thymidylate synthetase, affinity for DNA, and toxicity.

No correlation was obsd. between the tested mol. interactions of the diamidines and their effectiveness against *P. carinii* pneumonia.

ACCESSION NUMBER: 1990:151252 CAPLUS
 DOCUMENT NUMBER: 112:151252
 TITLE: Analogs of 1,5-bis(4-amidinophenoxy)pentane (pentamidine) in the treatment of experimental *Pneumocystis carinii* pneumonia
 AUTHOR(S): Tidwell, Richard R.; Jones, Susan Kilgore; Geratz, J. Dieter; Ohemeng, Kwasi A.; Cory, Michael; Hall, James Edwin
 CORPORATE SOURCE: Sch. Med., Univ. North Carolina, Chapel Hill, NC, 27599, USA
 SOURCE: Journal of Medicinal Chemistry (1990), 33(4), 1252-7
 CODEN: JMCMAR; ISSN: 0022-2623
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 112:151252
 IT 125880-66-2P

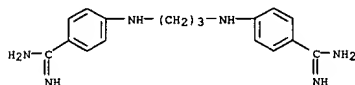
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. and hydrogenation of)

RN 125880-66-2 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediyldiimino)bis[3-nitro-, dihydrochloride] (9CI) (CA INDEX NAME)



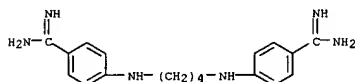
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IT 109563-82-8P 125880-64-0P 125880-65-1P
 125880-67-3P 125880-68-4P 125880-69-5P
 125880-70-8P 125880-73-1P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. and Pneumocystis carinii pneumonia inhibition by and toxicity of)
 RN 109563-82-8 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediylidimino)bis-, dihydrochloride (9CI) (CA INDEX NAME)



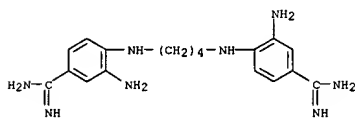
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RN 125880-64-0 CAPLUS
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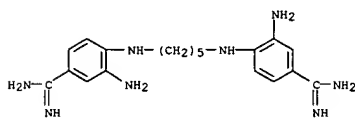
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RN 125880-65-1 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis-, dihydrochloride (9CI) (CA INDEX NAME)



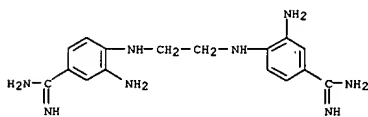
● 4 HCl

RN 125880-70-8 CAPLUS
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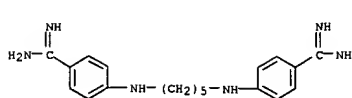
● 4 HCl

RN 125880-73-1 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,4-butanediylidimino)bis[3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)



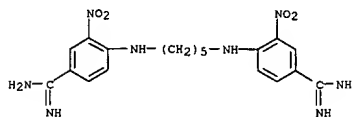
● 4 HCl

IT 124076-63-7 125880-81-1 125880-82-2
 125880-83-3 125880-84-4 125880-85-5
 125880-86-6 125880-87-7 125880-89-9
 RL: BIOL (Biological study)
 (Pneumocystis carinii pneumonia inhibition by and toxicity of)
 RN 124076-63-7 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis- (9CI) (CA INDEX NAME)



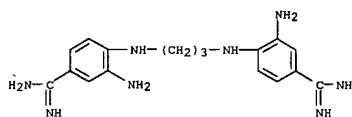
● 2 HCl

RN 125880-67-3 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro-, dihydrochloride (9CI) (CA INDEX NAME)



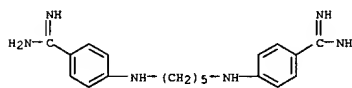
● 2 HCl

RN 125880-68-4 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediylidimino)bis[3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)

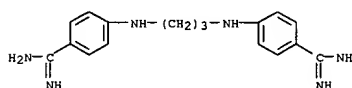


● 4 HCl

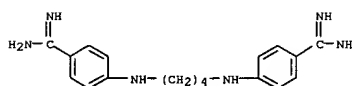
RN 125880-69-5 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,4-butanediylidimino)bis[3-amino-, tetrahydrochloride (9CI) (CA INDEX NAME)



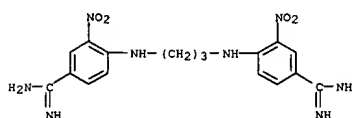
RN 125880-81-1 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediylidimino)bis- (9CI) (CA INDEX NAME)



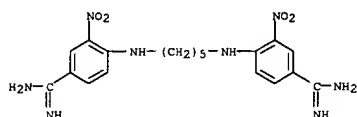
RN 125880-82-2 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,4-butanediylidimino)bis- (9CI) (CA INDEX NAME)



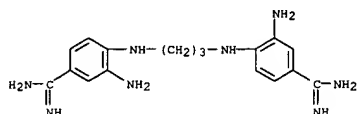
RN 125880-83-3 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediylidimino)bis[3-nitro- (9CI) (CA INDEX NAME)



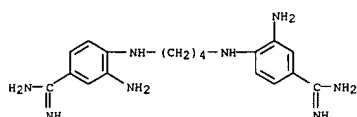
RN 125880-84-4 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,5-pentanediyldiimino)bis[3-nitro- (9CI) (CA INDEX NAME)



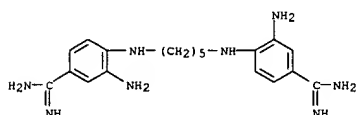
RN 125880-85-5 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,3-propanediylidimino)bis(3-amino- (9CI)
(CA INDEX NAME)



RN 125880-86-6 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,4-butanediylidimino)bis(3-amino- (9CI)
(CA INDEX NAME)



RN 125880-87-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanedylidimino)bis(3-amino- (9CI)
(CA INDEX NAME)

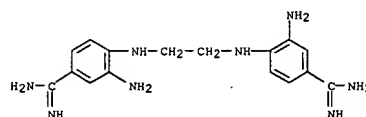
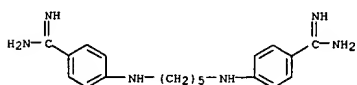


RN 125880-89-9 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,2-ethanediylidimino)bis(3-amino- (9CI)
(CA INDEX NAME)

L8 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2003 ACS

AB A HPLC method was developed for the detection and quantification of pentamidine and pentamidine analogs of chemotherapeutic value in order to measure their concn. in physiol. fluids. The compds. were extd. from urine over octadecyl solid-phase extn. columns, followed by chromatog. sepn. with an octadecyl reversed-phase column. For the mobile phase, a gradient of 31.5-37.5% MeCN in water, with Na heptanesulfonate and N(Me)4Cl as ion modifiers, was used. This method was used to reliably detect levels as low as 341 ng/mL without concn. of the compds. during the solid-phase extn. The assay was used to det. the effectiveness of several solid-phase extn. columns for isolating the compds. of interest and to quantify the amt. of pentamidine and its analogs contained in the urine of

dosed rats.
ACCESSION NUMBER: 1990:87 CAPLUS
DOCUMENT NUMBER: 112:87
TITLE: High-performance liquid chromatographic method for the quantification of several diamidine compounds with potential chemotherapeutic value
AUTHOR(S): Berger, Bradley J.; Hall, James Edwin; Tidwell, Richard R.
CORPORATE SOURCE: Sch. Public Health, Univ. North Carolina, Chapel Hill, NC, 27599, USA
SOURCE: Journal of Chromatography (1989), 494, 191-200
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 124076-63-7
RL: ANST (Analyte); ANST (Analytical study) (detr. of, in urine by HPLC)
RN 124076-63-7 CAPLUS
CN Benzenecarboximidamide, 4,4'-(1,5-pentanedylidimino)bis- (9CI) (CA INDEX NAME)

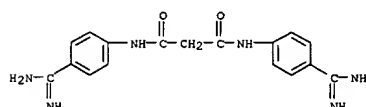


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AB Similarities and differences of trypsin (I) and plasma kallikrein (II) are

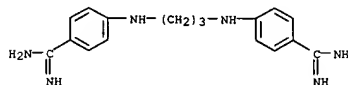
interpreted. Various amidines were tested for inhibition of II activity with N-.alpha.-tosyl-L-arginine Me ester (TAME) as substrate. Results with 150 amidines in vitro showed that aliphatic amidines were inactive. Some aromatic amidines, bis-amidines more than mono-amidines, had considerable inhibitory action. All amidines acted as competitive inhibitors. Substitution of the amidine group gave a loss of activity. Results are tabulated with structural formulas of 7 aromatic amidines inhibiting kallikrein for TAME substrate, and for 6 aromatic amidines inhibiting TAME hydrolysis by kallikrein, I, thrombin, and plasmin. Several amidines were tested against burns in guinea pigs and turpentine-induced edema in the pleural cavity of rats. The results varied with exptl. conditions, but some amidines had activity against the exptl. irritations. In general, the in vitro inhibitory activity of amidines was more specific than in vivo activity. Compd. I.C.I. 34,394, had marked activity against kallikrein, trypsin, thrombin, and plasmin in vitro.

ACCESSION NUMBER: 1971:120730 CAPLUS
DOCUMENT NUMBER: 74:120730
TITLE: Inhibition of guinea pig plasma kallikrein by amidines
AUTHOR(S): Davies, George Edward; Lowe, J. S.
CORPORATE SOURCE: Pharm. Div., Imp. Chem. Ind., Macclesfield/Cheshire, UK
SOURCE: Advances in Experimental Medicine and Biology (1970), 8, 453-60
CODEN: AEMBAP; ISSN: 0065-2598
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 32152-41-3
RL: BIOL (Biological study) (kallikreins inhibition by)
RN 32152-41-3 CAPLUS
CN Propanediamide, N,N'-bis[4-(aminoiminomethyl)phenyl]-, dihydrochloride (9CI) (CA INDEX NAME)



L8 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS
 AB cf. CA 55, 5521e. The title compds. and the piperazine deriv.,
 1,4-bis(p-amidinophenyl)piperazine (I) were described. They had no
 significant trypanocidal activity. p-Aminobenzamidine-HCl (8.5 g.) in 50
 ml. alc. and 2 ml. 40% HCHO refluxed 0.5 hr. gave 4.3 g.
 bis(p-amidinoanilino)methane-2HCl, m. 236-8.degree. (MeOH-Me2CO). CuCN
 (6.8 g.) and 10 ml. C5H5N heated to 120-30.degree., 9.25 g.
 1,2-bis(p-bromoanilino)ethane added, the temp. raised to 215-20.degree.,
 the C5H5N distd., the melt stirred at 195-200.degree. 3 hrs., added to 20
 g. KCN in 50 ml. H2O (the oil sepd. and hardened), the liquor poured off,
 the mass ground with 2N HCl to give 14.5 g. solid, this sublimed, and the
 yellow sublimate (300-10.degree./0.1 mm.) (0.45 g.) crystd. gave 0.33 g.
 1,2-bis(p-cyanoanilino)ethane (II), m. 205-6.degree. (AcOH).
 p-Aminobenzonitrile (100 g.), 142 g. NaHCO3, 160 g. C2H4Br2, and 400 ml.
 EtOCH2CH2OH refluxed 18 hrs., the mixt. cooled to 10.degree., the insol.
 material removed, the filtrate dild. with H2O, and the brown granular
 solid collected, p-Aminobenzonitrile (51 g.) was recovered from the
 mother liquors. The brown solid crystd. gave 18 g. product, sublimed to
 afford 9 g. II. The 1st filtered product afforded 6.6 g.
 1,4-bis(p-cyanophenyl)piperazine (III), yellow needles, m. 275-7.degree.
 (anisolet). p-Aminobenzonitrile (5 g.), 4.25 g. anhyd. Na2CO3, and 7.1 g.
 C2H4Br2 refluxed 3 hrs. at 150-5.degree., cooled, filtered, and the solid
 crystd. gave 1.4 g. III. II (27.5 g.) in 650 ml. EtOCH2CH2OH at
 0-5.degree. satd. with HCl, left 10 days and the mixt. treated with 390
 ml. satd. alc. NH3 at 55-60.degree. gave 7.5 g. 1,2-bis(p-
 aminoanilino)ethane-2HCl (IV), plates, m. 353.degree. (decompn.) IV (7.5
 g.) in 800 ml. H2O treated at 10-15.degree. with 50% NaOH gave 6.4 g.
 product, which suspended in 80 ml. MeOH with methanesulfonic acid gave
 7.1 g. 1,2-bis(p-amidinoanilino)ethane di(methanesulfonate), m.
 301-2.degree. (MeOH). III (8.4 g.) in 150 ml. EtOCH2CH2OH satd. at 0.5.degree. with
 HCl gave 1.2HCl. I. 2HCl (6 g.) in 750 ml. H2O basified and the base treated
 with 20 ml. 2N isethionic acid gave 5.5 g. I diisethionate, yellow
 needles, m. 328.degree. (decompn.) (MeOH). p-Aminobenzonitrile (12 g.)
 in 100 ml. 2N HCl and 150 ml. H2O stirred 1 hr. with 12 ml.
 1,1,3,3-tetraethoxypropane, the 15 g. solid washed, and a soln. in 300
 ml. 96% aq. C5H5N treated with 300 ml. H2O gave 11 g.
 1-(p-cyanoanilino)-3-(p-cyanophenylimino)-1-propene, m. 227-9.degree.. p-Aminobenzonitrile (11.8
 g.), 5.2 ml. 1,3-dibromopropane, 8.4 g. NaHCO3, and 50 ml. EtOCH2CH2OH
 refluxed overnight gave 3 g. 1,3-bis(p-cyanoanilino)propane (V), m.
 159-61.degree. (aq. alc.). 1-(p-Cyanoanilino)-3-(p-cyanophenylimino)-1-
 propene (11 g.) in 700 ml. HCONMe2 hydrogenated at room temp. with 1.6 g.
 PtO2 1.5 hrs. gave 4.15 g. V. 1,3-Bis(p-cyanoanilino)propane (10 g.) in
 200 ml. alc. satd. with HCl at 0-5.degree. and the diimidoester-2HCl
 which sepd. during 1 week (14.1 g.) dissolved in 100 ml. refluxing H2O and 30
 ml. satd. NaCl gave 5.8 g. 1,3-bis(p-amidoanilino)propane-2HCl, yellow
 plates, m. 316-18.degree. (decompn.). Na glutaric aldehyde-2H2O (1.55
 g.) in 50 ml. H2O added at 80-90.degree. to 2.36 g. p-aminobenzonitrile
 in 20 ml. 2N H2SO4 and 120 ml. H2O, the mixt. stirred a further 10 min., and
 filtered gave 2.5 g. 1-(p-cyanoanilino)-5-(p-cyanophenylimino)-1,3-
 pentadiene, m. 140-4.degree. (decompn.), which (2.4 g.) in 100 ml.
 HCONMe2 reduced at 30-5.degree. over 0.24 g. PtO2, the ppt. filtered off, washed,
 and extd. with CHCl3 gave 1.8 g. brown solid, m. 160-70.degree..
 Attempts

L8 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2003 ACS (Continued)
 to purify this product were unsuccessful. The aq. dimethylformamide
 filtrate gave 0.2 g. p-aminobenzonitrile. p-Aminobenzonitrile (94.4 g.),
 97.6 g. hexamethylene dibromide, 67.2 g. NaHCO3, 400 ml. EtOCH2CH2OH, and
 a crystal of iodine refluxed 24 hrs., the solvent evapd., the residual
 oil cooled, stirred with 2 l. 2N HCl, extd. with CHCl3, and the solvent
 removed gave 16 g. 1,6-bis(p-cyanoanilino)hexane (VI), prismatic needles,
 m. 165-7.degree. (AcOH). Similarly, 15 g. VI in 180 ml. EtOCH2CH2OH
 satd. at 0-5.degree. with HCl gave the di-HCl salt, converted to 5.2 g.
 1,6-bis(p-amidinoanilino)hexane diisethionate, prisms, m. 238-40.degree.
 (H2O and MeOH).
 ACCESSION NUMBER: 1961:43097 CAPLUS
 DOCUMENT NUMBER: 55:43097
 ORIGINAL REFERENCE NO.: 55:8344c-1,8345a-b
 TITLE: Search for chemotherapeutic amidines. XVII.
 .alpha.,.omega.-Bis(p-amidinoanilino)alkanes
 AUTHOR(S): Berg, S. S.
 CORPORATE SOURCE: Northern Polytechnic, London
 SOURCE: J. Chem. Soc. (1960) 5172-6
 DOCUMENT TYPE: Journal
 LANGUAGE: Unavailable
 IT 109563-82-8, Benzamidine, 4,4'-(trimethylenediimino)di-,
 dihydrochloride
 (prepn. of)
 RN 109563-82-8 CAPLUS
 CN Benzenecarboximidamide, 4,4'-(1,3-propanediylidimino)bis-,
 dihydrochloride
 (9CI) (CA INDEX NAME)



● 2 HCl

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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

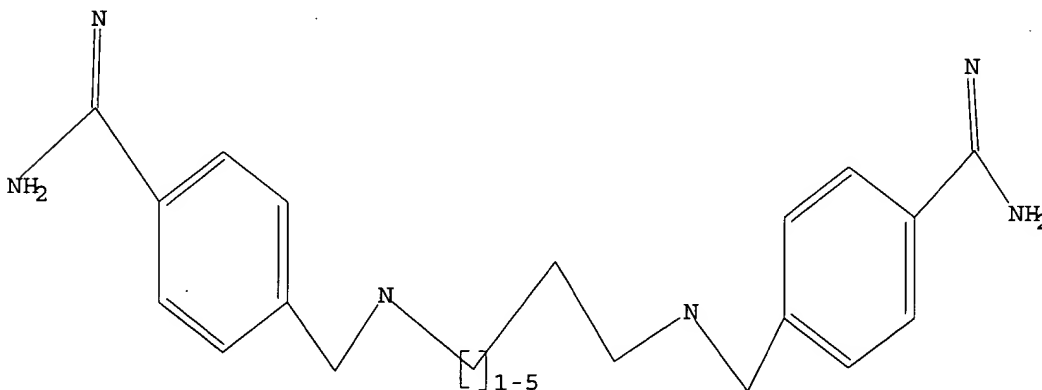
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L9 STRUCTURE UPLOADED

=> d query

L9 STR



Structure attributes must be viewed using STN Express query preparation.

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SAMPLE SCREEN SEARCH COMPLETED - 17 TO ITERATE

100.0% PROCESSED 17 ITERATIONS 0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 93 TO 587
PROJECTED ANSWERS: 0 TO 0

L10 0 SEA SSS SAM L9

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FULL SCREEN SEARCH COMPLETED - 433 TO ITERATE

100.0% PROCESSED 433 ITERATIONS 3 ANSWERS
SEARCH TIME: 00.00.01

L11 3 SEA SSS FUL L9

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	ENTRY	SESSION
FULL ESTIMATED COST	148.15	564.27
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	ENTRY	SESSION
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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l11
L12 5 L11

=> d l12 1-5 abs ibib hitstr

L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB Polyamine or polyamine analog-amino acid conjugates
(M)-N(E)-(B-A-B-NH)4-E

or (M)-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [M is an amino acid; A is a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B is a bond, alkyl, or alkenyl; E is H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl], including salts or stereoisomers, were prep'd. for use as antiviral agents.

An example is the polyamine glutamine conjugate SL-11165 [NH₂CH(CH₂CH₂CONH₂)CON(Et)(CH₂CH₂CH₂CH₂NH)4Et.bul.5HCl]. Thus, (E)-EtNH(CH₂)4NHCH₂CH₂CHCH₂NH(CH₂)4NH₂ was prep'd. by a multi-step sequence starting from 4-bromobutanenitrile, N-(mesitylsulfonyl)ethanamine, and (E)-2-butene-1,4-diol.

ACCESSION NUMBER: 2002:888472 CAPLUS

DOCUMENT NUMBER: 137:384565

TITLE: Preparation of polyamine or polyamine analog-amino acid conjugates as antiviral agents

INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.; Gutierrez, Jesus A.

PATENT ASSIGNEE(S): S111 Biomedical Corporation, USA; Eli Lilly & Company

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002091989	A2	20021121	WO 2001-US43887	20011108
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DS, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: US 2000-246804P P 20001108

OTHER SOURCE(S): MARPAT 137:384565

IT 304911-05-5P, SL 11137 304911-11-3P, SL 11134

304911-12-4P, SL 11136

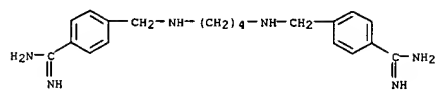
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of polyamine or polyamine analog-amino acid conjugates as antiviral agents)

RN 304911-05-5 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

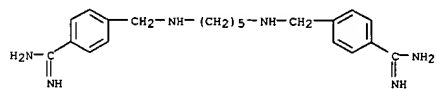
L12 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)



● 4 HCl

RN 304911-11-3 CAPLUS

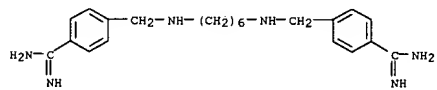
CN Benzenecarboximidamide, 4,4'-[1,5-pentanediybis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

RN 304911-12-4 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS

AB Conjugates of polyamines analogs conjugated to at least one amino acid of formula M-N(E)-(B-A-B-NH)4-E or M-N(E)-(B-A-B-NH)3-B-A-B-N(M)-E [wherein

M

= independently an amino acid, esp. glutamine, asparagine, lysine, ornithine, arginine, histidine, or citrulline; A = independently a bond, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; B = independently a bond, alkyl, or alkenyl; E = independently H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, or cycloaryl; and salts or stereoisomers thereof]

were tested and claimed for pharmaceutical use as anticancer agents. For example, the polyamine glutamine conjugate SL-11165 [NH₂CH(CH₂CH₂CONH₂)CON(Et)(CH₂CH₂CH₂CH₂NH)4Et.bul.5HCl] exhibited ID50 values of >31.65, 4.1, and >31.25 against the DuPro, PC-3, and LnCap prostate cancer cell lines, resp. In addn., conformationally restricted polyamine analogs were prep'd. Thus,

(E)-EtNH(CH₂)4NHCH₂CH₂CHCH₂NH(CH₂)4NH

Et was prep'd. in a multi-step sequence starting from 4-bromobutanenitrile,

N-mesitylethanamine, and (E)-2-butene-1,4-diol.

ACCESSION NUMBER: 2002:368258 CAPLUS

DOCUMENT NUMBER: 136:386292

TITLE: Preparation of conformationally restricted polyamine analogs and use of polyamine amino acid conjugates as anticancer agents

INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Valasinas, Aldonia L.; Reddy, Venodhar K.

PATENT ASSIGNEE(S): S111 Biomedical Corporation, USA

SOURCE: PCT Int. Appl., 74 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002038105	A2	20020516	WO 2001-US43585	20011108
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DS, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

AU 2002038126 A5 20020521

PRIORITY APPLN. INFO.: US 2000-246804P P 20001108

WO 2001-US43585 W 20011108

OTHER SOURCE(S): MARPAT 136:386292

IT 304911-05-5P, SL 11137 304911-12-4P, SL 11136

RL: SPN (Synthetic preparation); PREP (Preparation)

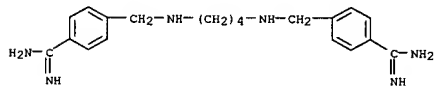
(polyamine; prep'n. of conformationally restricted polyamines and use

of polyamine amino acid conjugates as anticancer agents)

RN 304911-05-5 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

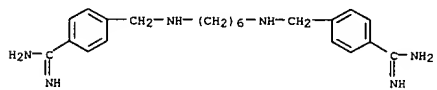
L12 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)



● 4 HCl

RN 304911-12-4 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,6-hexanediylbis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS
AB Microsporidia are eukaryotic obligate intracellular protists that are emerging pathogens in immunocompromised hosts, such as patients with AIDS or patients who have undergone organ transplantation. We have demonstrated in vitro and in vivo that synthetic polyamine analogs are effective anticrosporidial agents with a broad therapeutic window. CD8-knockout mice or nude mice infected with the microsporidian Encephalitozoon cuniculi were cured when they were treated with four different novel polyamine analogs at doses ranging from 1.25 to 5 mg/kg

of body wt./day for a total of 10 days. Cured animals demonstrated no evidence of parasitemia by either PCR or histol. staining of tissues 30 days after untreated control animals died.

ACCESSION NUMBER: 2002:30291 CAPLUS

DOCUMENT NUMBER: 136:318859

TITLE: Novel synthetic polyamines are effective in the treatment of experimental microsporidiosis, an opportunistic AIDS-associated infection
AUTHOR(S): Bacchi, Cyrus J.; Weiss, Louis M.; Lane, Schenella; Frydman, Benjamin; Valasinas, Aldonia; Reddy, Venodhar; Sun, Jerry S.; Marton, Laurence J.; Khan, Imtiaz A.; Moretto, Magali; Yarett, Nigel; Wittner, Murray
CORPORATE SOURCE: Haskins Laboratories and Departments of Biology and Chemistry, Pace University, New York, NY, 10038-1598, USA

SOURCE: Antimicrobial Agents and Chemotherapy (2002), 46(1), 55-61
CODEN: AMACQ; ISSN: 0066-4804

PUBLISHER: American Society for Microbiology

DOCUMENT TYPE: Journal

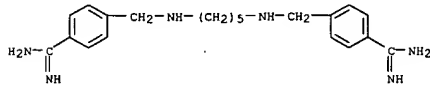
LANGUAGE: English

IT 304911-11-3, SL 11134

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11134: novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

RN 304911-11-3 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,5-pentanediyldis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

IT 304911-12-4, SL 11136

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11136: novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

RN 304911-12-4 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,6-hexanediyldis(aminomethylene)]bis-,

L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS
AB Novel conformationally restricted polyamines, such as E-NH-(B-A-B-NH)4-E [A, E = bond, alkyl, alkenyl, alkynyl, cycloalkyl, cycloaryl, cycloalkenyl; B = bond, alkyl, alkenyl], were prepd. for pharmaceutical use as anticancer agents. Thus, (E)-E₁NH(CH₂)₄NHCH₂CH:CHCH₂NH(CH₂)₄NHET was prepd. in a multistep sequence starting from mesityl chloride 4-bromobutanenitrile, N-mesitylthalamine, and (E)-2-butene-1,4-diol.

The prepd. polyamines were tested for antiproliferative activity against human prostate cancer cell lines, such as PC3 and DUPRO.

ACCESSION NUMBER: 2000:790505 CAPLUS

DOCUMENT NUMBER: 133:350095

TITLE: Preparation of conformationally restricted polyamine analogs as disease therapies
INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.; Reddy, Venodhar K.; Valasinas, Aldonia; Blokhin, Andrei V.; Basu, Hrak S.

PATENT ASSIGNEE(S): Slll Biomedical Corporation, USA

SOURCE: PCT Int. Appl., 135 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066587	A2	20001109	WO 2000-US11591	20000427
WO 2000066587	A3	20010125		
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1177197	A2	20020206	EP 2000-928583	20000427
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010701	A	20020213	BR 2000-10701	20000427
JP 2002543202	T2	20021217	JP 2000-615617	20000427
PRIORITY APPLN. INFO.: US 1999-131779P P 19990430				
WO 2000-US11591 W 20000427				

OTHER SOURCE(S): MARPAT 133:350095

IT 304911-05-5P, SL 11137 304911-11-3P, SL 11134

304911-12-4P, SL 11136

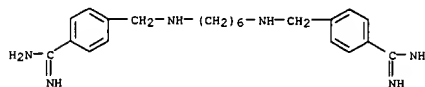
RL: BAC (Biological activity or effector, except adverse); BSU

(Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of conformationally restricted polyamines as antiproliferative prostate cancer agents)

RN 304911-05-5 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

L12 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)
tetrahydrochloride (9CI) (CA INDEX NAME)



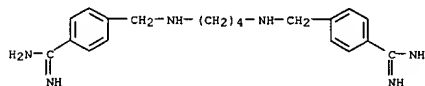
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IT 304911-05-5, SL 11137

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(SL 11137: novel synthetic polyamines are effective in treatment of exptl. microsporidiosis, opportunistic AIDS-assocd. infection)

RN 304911-05-5 CAPLUS

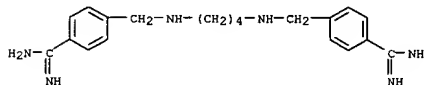
CN Benzenecarboximidamide, 4,4'-[1,4-butanediylbis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

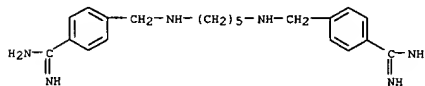
L12 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2003 ACS (Continued)



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RN 304911-11-3 CAPLUS

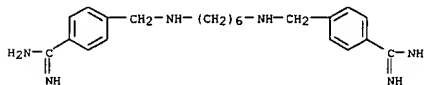
CN Benzenecarboximidamide, 4,4'-[1,5-pentanediyldis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

RN 304911-12-4 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,6-hexanediyldis(aminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

L12 ANSWER 5 OF 5 CAPLUS- COPYRIGHT 2003 ACS

AB The invention relates to peptide conjugates in which cytotoxic and cytostatic agents, such as polyamine analogs or naphthoquinones, are conjugated to a polypeptide recognized and cleaved by enzymes such as prostate-specific antigen (PSA) and cathepsin B. Methods of using these conjugates in the treatment of prostate diseases are also provided.

Thus, C2[CH2NH(CH2)4NHET]2.4HCl (SL-11103), 4-[[7-[4-(9-acridinylamino)phenyl]heptyl]oxy]-1,2-naphthoquinone (SL-11064), and morpholino-Ser-Lys-Leu-Gln- β -Ala- β -lapachone (SL-11147) were prepd. and assayed for antitumor activity against human prostate cancer cell lines, such as PC-3 and DUPRO.

ACCESSION NUMBER: 2000:790358 CAPLUS

DOCUMENT NUMBER: 133:350515

TITLE: Preparation of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases

INVENTOR(S): Frydman, Benjamin; Marton, Laurence J.

PATENT ASSIGNEE(S): S111 Biomedical Corporation, USA

SOURCE: PCT Int. Appl., 194 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000066175	A2	20001109	WO 2000-US11542	20000427
WO 2000066175	A3	20010802		
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RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GN, GW, GM, ML, MR, NE, SN, TD, TG			
EP 1173223	A2	20020123	EP 2000-928565	20000427
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
BR 2000010700	A	20020213	BR 2000-10700	20000427
JP 2002543163	T2	20021217	JP 2000-615058	20000427
PRIORITY APPLN. INFO.:			US 1999-131809P	P 19990430
			WO 2000-US11542	W 20000427

OTHER SOURCE(S): MARPAT 133:350515

IT 304911-11-3P, SL 11134 304911-12-4P, SL 11136

RL: BAC (Biological activity or effector, except adverse); BSU

(Biological

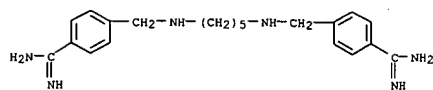
study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)

RN 304911-11-3 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,5-pentanediy]bis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)

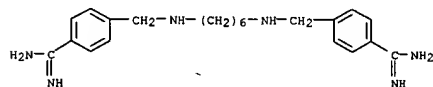
L12 ANSWER 5 OF 5 CAPLUS- COPYRIGHT 2003 ACS (Continued)



● 4 HCl

RN 304911-12-4 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,6-hexanediy]bis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

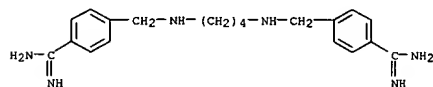
IT 304911-05-5P, SL 11137

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(prepn. of novel polyamine analog conjugates and quinone conjugates as therapies for cancers and prostate diseases)

RN 304911-05-5 CAPLUS

CN Benzenecarboximidamide, 4,4'-[1,4-butanediyl]bis(iminomethylene)]bis-, tetrahydrochloride (9CI) (CA INDEX NAME)



● 4 HCl

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COST IN U.S. DOLLARS

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FULL ESTIMATED COST

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589.04

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

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SESSION

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DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

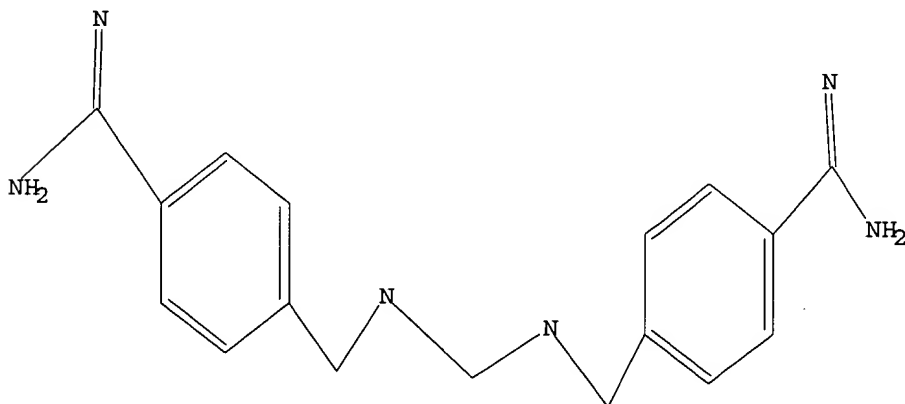
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L13 STR



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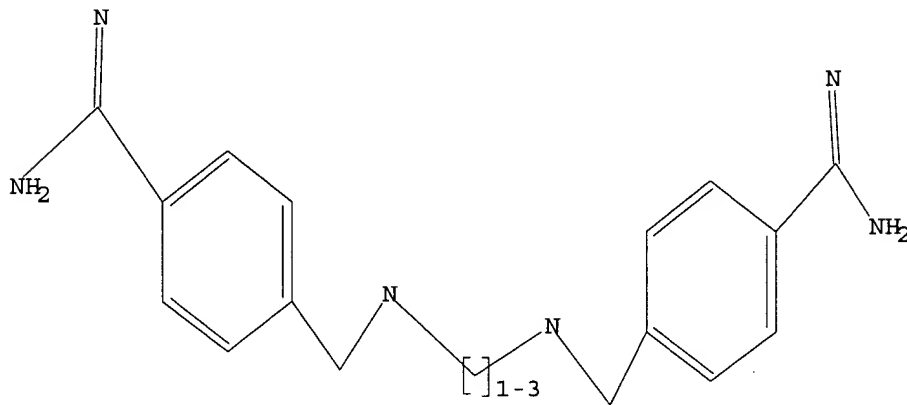
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SEARCH TIME: 00.00.01

L18 2 SEA SSS FUL L16

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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

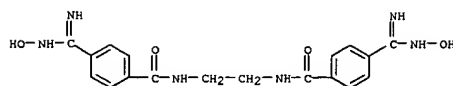
AB Arom. dicationic compds., such as pentamidine, have potent antimicrobial activities. Clin. use of these compds. has been restricted, however, by their toxicity and limited oral activity. A novel approach, using amidoxime derivs. as prodrugs, has recently been proposed to overcome these limitations. Although results were presented for amidoxime derivs. of only one diamidine, pentamidine, the authors in the original proposal claimed that amidoxime derivs. would work as effective prodrugs for all pharmacol. active diamidines. Nine novel amidoxime derivs. were synthesized and tested in the present study for activity against *Pneumocystis carinii* in corticosteroid-suppressed rats. Only three of

the nine compds. had significant oral anti-*Pneumocystis* activity. The bisbenzamidoxime derivs. of three direct pentamidine analogs had excellent oral and i.v. activities and reduced acute host toxicity. These compds. are not likely candidates for future drug development, however, because they have chronic toxic effects and the active amidine compds. have multiple sites susceptible to oxidative metab., which complicates their pharmacol. and toxicol. Novel diamidoximes from three other structural classes, contg. different groups linking the cationic moieties, lacked significant oral or i.v. anti-*Pneumocystis* activity, even though the corresponding diamidines were very active i.v. Both active and inactive amidoximes were readily metabolized to the corresponding amidines by cell-free liver homogenates. Thus, the amidoxime prodrug approach may provide a strategy to exploit the potent antimicrobial and other pharmacol. activities of selected, but certainly not all, arom. diamidines.

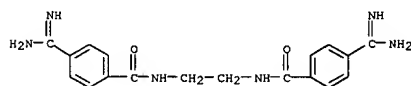
ACCESSION NUMBER: 1998:189774 CAPLUS
DOCUMENT NUMBER: 128:303628
TITLE: Anti-*Pneumocystis* activities of aromatic diamidoxime prodrugs
AUTHOR(S): Hall, James Edwin; Kerrigan, John E.; Ramachandran, Kishore; Bender, Brendan C.; Stanko, Jason P.; Jones, Susan K.; Patrick, Donald A.; Tidwell, Richard R.
CORPORATE SOURCE: Department of Epidemiology, University of North Carolina at Chapel Hill, Chapel Hill, NC, 27599, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1998), 42(3), 666-674
CODEN: AMACCO; ISSN: 0066-4804
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

IT 206532-31-2P
RL: BAC (Biological activity or effector, except adverse); BPR
(Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(anti-*Pneumocystis* activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)
RN 206532-31-2 CAPLUS
CN Benzamide, N,N'-1,2-ethanediylbis[4-[(hydroxyamino)iminomethyl]- (9CI)
(CA INDEX NAME)

L19 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS (Continued)



IT 206532-32-3P
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(anti-*Pneumocystis* activities of arom. diamidoxime prodrugs in relation to structure and metab. and toxicity)
RN 206532-32-3 CAPLUS
CN Benzamide, N,N'-1,2-ethanediylbis[4-(aminoiminomethyl)- (9CI) (CA INDEX NAME)



=> fil reg

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

5.79

891.13

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE

TOTAL

ENTRY

SESSION

CA SUBSCRIBER PRICE

-0.65

-20.19

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STRUCTURE FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STN Note 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

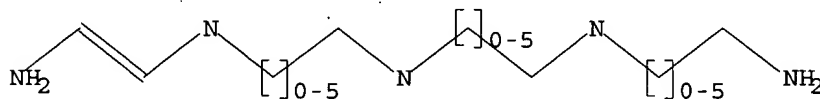
=>

Uploading 09560711.str

L20 STRUCTURE UPLOADED

=> d query

L20 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l20

SAMPLE SEARCH INITIATED 16:39:51 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 3553 TO ITERATE

28.1% PROCESSED 1000 ITERATIONS

0 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 67487 TO 74633

PROJECTED ANSWERS: 0 TO 0

L21 0 SEA SSS SAM L20

=> s l20 full

FULL SEARCH INITIATED 16:40:01 FILE 'REGISTRY'

FULL SCREEN SEARCH COMPLETED - 72286 TO ITERATE

100.0% PROCESSED 72286 ITERATIONS

0 ANSWERS

SEARCH TIME: 00.00.02

L22 0 SEA SSS FUL L20

=>

Uploading 09560711.str

L23 STRUCTURE UPLOADED

=> d queyr

L23 HAS NO ANSWERS

'QUEYR ' IS NOT A VALID STRUCTURE FORMAT KEYWORD

Structure Formats

SIA ----- Structure Image, Attributes, and map table if it contains data. (Default)

SIM ----- Structure Image.

SAT ----- Structure ATtributes and map table if it contains data.

SCT ----- Structure Connection Table and map table if it contains data.

SDA ----- All Structure Data (image, attributes, connection table and map table if it contains data).

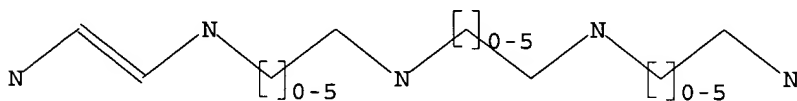
NOS ----- NO Structure data.

ENTER STRUCTURE FORMAT (SIM), NOS:nos

L23 STR

=> d query

L23 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l23

SAMPLE SEARCH INITIATED 16:41:20 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 3553 TO ITERATE

28.1% PROCESSED 1000 ITERATIONS

0 ANSWERS

INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)

SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

BATCH **COMPLETE**

PROJECTED ITERATIONS: 67487 TO 74633

PROJECTED ANSWERS: 0 TO 0

L24 0 SEA SSS SAM L23

=> s 23 full
L25 460971 23

=> s 123
SAMPLE SEARCH INITIATED 16:41:46 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 3553 TO ITERATE

28.1% PROCESSED 1000 ITERATIONS 0 ANSWERS
INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED)
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 67487 TO 74633
PROJECTED ANSWERS: 0 TO 0

L26 0 SEA SSS SAM L23

=> s 123 full
FULL SEARCH INITIATED 16:41:54 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 72286 TO ITERATE

100.0% PROCESSED 72286 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

L27 6 SEA SSS FUL L23

=> fil caplus		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	304.12	1195.25
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-20.19

FILE 'CAPLUS' ENTERED AT 16:42:02 ON 06 FEB 2003
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FILE COVERS 1907 - 6 Feb 2003 VOL 138 ISS 6
FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l27

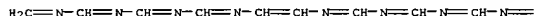
L28 3 L27

=> d l28 1-3 abs ibib hitstr

of (HCN)_n .cntdot.cntdot.cntdot. HCCH .cntdot.cntdot.cntdot. (NCH)_n
(n = 2-4) and for the corresponding n = 2 dianion.

ACCESSION NUMBER: 2000:508846 CAPIUS
DOCUMENT NUMBER: 133:286775
TITLE: Bi-dipole-bound anions
AUTHOR(S): Gutowski, M.; Skurski, P.; Simons, J.
CORPORATE SOURCE: Materials Resources, Pacific Northwest National Laboratory, Richland, WA, 99352, USA
SOURCE: International Journal of Mass Spectrometry (2000), 201(1-3), 245-252
CODEN: IMSPF8; ISSN: 1387-3806
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
IT 300347-22-2
RL: PRP (Properties)
(electronic structure and electron attachment energy of)
RN 300347-22-2 CAPIUS
CN Methanimidamide,
N',N''-1,2-ethenediylbis[N-[[[(methyleneamino)methylene]amino)methylene]-9CI] (CA INDEX NAME)

PAGE 1-A

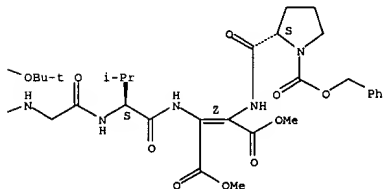


PAGE 1-B



FORMAT

PAGE 1-B

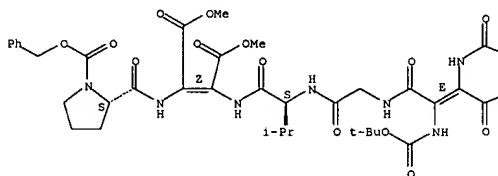


FORMAT

ACCESSION NUMBER: 2000:447433 CAPLUS
DOCUMENT NUMBER: 133:208164
TITLE: Stereocontrolled backbone connection of peptides by C=C-double bonds
AUTHOR(S): Schumann, Susanne; Zeitler, Kirsten; Jager, Martin; Polborn, Kurt; Steglich, Wolfgang
CORPORATE SOURCE: Department Chemie der Ludwig-Maximilians-Universitaet Muenchen, Muenchen, D-81377, Germany
SOURCE: Tetrahedron (2000), 56 (25), 4187-4195
CODEN: TETRA8; ISSN: 0040-4020
PUBLISHER: Elsevier Science Ltd.
LANGUAGE: English
OTHER SOURCE(S): CASREACT 133:208164

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

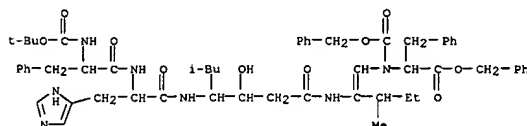


C5-10
cycloalkoxy[alkylene]; R3 = OH, amino, acylamino, alkoxy, alkoxycarbonyl;
R1 = amino, Cl-4 alkoxy, 4-benzylpiperazin-1-yl, 1,2,3,4-
tetrahydroquinolin-1-yl, A-E-B, etc.; A = Lys, Pro, Ile; E = Phe, Gly,
Ala, Val, Ile, Lys, Orn, Arg, Asp, etc.; B = OH, alkoxy, amino, glutamyl,
etc.) and their salts were prep'd. as renin inhibitors.
BOC-Phe-His-Sta-Ile-Sta-OH (StA = 4S-amino-3S-hydroxy-6-methylheptanoyl).
Prep'd by the soln. phase method, inhibited renin with an IC50 of <4

as renin inhibitors
INVENTOR(S): Bindra, Jasit S.; Kleinman, Edward F.; Rosati, Robert L.
PATENT ASSIGNEE(S): Pfizer Inc., USA
SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 763,768, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4749687	A	19880607	US 1986-839010	19860310
CA 1254699	A1	19890523	CA 1985-476191	19850311
PRIORITY APPLN. INFO.:			US 1984-588279	19840312
			CA 1985-476191	19850311
			US 1985-763768	19850808

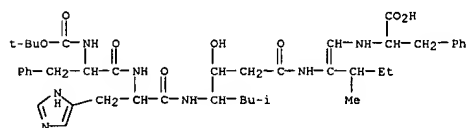
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (prepn. and hydrogenolysis of, in prepn. of renin inhibitor)
 116384-89-7 CARLUS
 CN L-histidinamide-1-[[1,1-dimethylethoxy]carbonyl]-1-phenylalanyl-N-[2-
 hydroxy-4-[[2-methyl-1-[[[2-oxo-2-(phenylethoxy)-1-
 (phenylethyl)ethyl]-[[phenylethoxy]carbonyl]amino]methyl]butyl]amino]-
 1,2-dimethylethyl]-4-oxobutyl]-, [15-1IR*,2R*,4(R*,R*)]- (5C1) [CA
 INDEX NAME]



RL: SPN (Synthetic preparation); PREP (Preparation)
 (prepn. of, as intermediate for renin inhibitor)
 IT 118403-86-4P 118403-87-5P
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological
 study, unclassified); SPN (Synthetic preparation); BIOL (Biological
 study); PREP (Preparation)
 (prepn. of, as renin inhibitor)
 RN 118403-86-4 CAPLUS
 CN L-Histidinamide,
 N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl-N-[4-[[1-
 [[(1-carboxy-2-phenylethylamino)methylene]-2-methylbutylamino]-2-hydroxy-
 1-(2-methylpropyl)-4-oxobutyl]-, [1S-[1R*,2R*,4[R*(R*)]]]-, monoacetate
 (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 118403-85-3
 CMF C43 H61 N7 O8

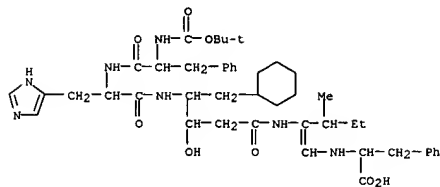


CM 2

CRN 64-19-7
 CMF C2 H4 O2



RN 118403-87-5 CAPLUS
 CN L-Phenylalanine, N-[2-[[[5-cyclohexyl-2,4,5-trideoxy-4-[[N-[N-[(1,1-dimethylethoxy)carbonyl]-L-phenylalanyl]-L-histidyl]amino]-L-threo-
 pentonoyl]amino]-3-methyl-1-pentenyl]-, (S)- (9CI) (CA INDEX NAME)



=> fil reg

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	14.03	1209.28
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-1.95	-22.14

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DICTIONARY FILE UPDATES: 5 FEB 2003 HIGHEST RN 486392-61-4

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when
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Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP
PROPERTIES for more information. See STN Note 27, Searching Properties
in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> fil caplus

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	2.00	1211.28
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-22.14

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FILE LAST UPDATED: 5 Feb 2003 (20030205/ED)

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```
=> s polyamine
      28502 POLYAMINE
      29335 POLYAMINES
L29   40432 POLYAMINE
      (POLYAMINE OR POLYAMINES)
```

```
=> s conformation?
L30   294106 CONFORMATION?
```

```
=> s l29 and l30
L31   672 L29 AND L30
```

=> logoff y		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	4.28	1215.56
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-22.14

STN INTERNATIONAL LOGOFF AT 16:46:58 ON 06 FEB 2003